THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

VOL. XXIX APRIL, 1933 No. 4

HYPERTROPHY OF THE PYLORIC MUSCLE OF ADULTS: A DISTINCTIVE ROENTGENOLOGIC SIGN*

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ALTHOUGH lesions at or near the pylorus are seldom difficult to discover by means of the roentgen ray, they are extraordinarily hard to identify specifically, for carcinoma, benign ulcer, syphilis, and hypertrophy of the pyloric muscle, which are the most common lesions encountered in this situation, usually produce perplexingly similar roentgenologic manifestations. During recent months, however, we have observed a roentgenologic phenomenon in cases of pyloric muscular hypertrophy which seemed to be pathognomonic of the condition. In order to verify this observation and to elicit further information bearing on the incidence, etiology and pathology of pyloric hypertrophy, we have reviewed 81 cases in which examination was made by means of the roentgen ray and presence of the condition confirmed, in the five years from 1927 to 1931 inclusive.

Excluding normal variations in thickness of the pyloric muscle, the incidence of clinically or surgically significant hypertrophy is relatively low. It would appear, however, that this infrequency has been overemphasized, for the aggregate of cases seen at The Mayo Clinic alone is not inconsiderable. At all events, it occurs sufficiently often to warrant consideration in the differential diagnosis of any stenotic lesion at the pylorus.

The cause of hypertrophic pyloric stenosis of adults is not definitely known, and it has been the subject of much speculation. Chief among hypotheses as to its etiology are that it is a continuance of infantile congenital stenosis into adult life, and that it is acquired by adults as a result of long maintained spasm of the pyloric sphincter. Kaufmann has said that it may be an original anomaly of development, a tumor-like hyperplasia of muscle, or an effect of spasm. This assumption of pylorospasm with a congenital background and consequent hypertrophy is shared by many, he has stated. Certain observers have expressed the belief that the spasm has an endocrine basis, and hyperadrenalism has been suggested as a causative factor. It is well known that pyloric spasm is often associated not only with intragastric disease, especially gastric ulcer, but with chronic cholecystitis, appendicitis, and other extragastric disease. By experiments on animals, Thomas and Wheelon have shown that stimulation of almost any visceral afferent nerve will induce pylorospasm. Similar results had been obtained previously by Carnot. Among potential

* Read at the Thirty-third Annual Meeting, American Roentgen Ray Society, Detroit, Mich., Sept. 27–30, 1932.

causes of pyloric hypertrophy Chomet mentioned duodenal and gastric ulcer, gastric carcinoma and chronic cholecystitis. Of the 4 cases reported by McClure, 2 appeared to be of the congenital type, but in the other 2 evidence indicated that the condition may have been related to peptic ulcer.

From our series of cases data which may be pertinent to the etiology were as follows: of the 81 patients, 65 were men and 16 women, a ratio comparable to that obtaining in other gastrointestinal diseases. Ten patients were from twenty-one to thirty years of age, 21 were in the fourth decade of life, 23 in the fifth, 19 in the sixth, and 8 were more than sixty years of age. These statistics seem to indicate that pyloric hypertrophy of adults occurs predominantly at middle age.

In 50 cases the hypertrophy was associated with other disease, as follows: 10 cases with duodenal ulcer, 4 with duodenal ulcer and duodenitis, 2 with duodenal ulcer and chronic cholecystitis with gallstones, 5 with duodenitis only, 12 with gastric ulcer, 1 with gastric ulcer and duodenal ulcer, 1 with gastric carcinoma, 7 with chronic cholecystitis and gallstones, 3 with chronic cholecystitis only, and 5 with chronic or subacute appendicitis. If it is assumed that the associated lesions preceded the hypertrophy, the hypothesis that pyloric hypertrophy commonly results from reflex pylorospasm would have additional support. But the order of sequence is not known, and it could be contended more or less plausibly that stasis induced by the hypertrophy led to the production of gastric or duodenal disease. The series does indicate, however, that in the majority of cases pyloric hypertrophy is associated with duodenal, gastric, or cholecystic disease, and in this order of frequency.

a *b* *c*

Fig. 1. Three typical cases of uncomplicated hypertrophy of the pyloric muscle. The characteristic concave indentation of the bulbar base is apparent in each case. In the case illustrated in *b*, the surgeon said that the hypertrophy was more extensive than any he had seen previously. In the third case, *c*, the transverse rugae of the antrum are accentuated.

As to the morbid anatomy of hypertrophic pyloric stenosis, Kaufmann wrote: "The pylorus becomes a tube from 2 to 3 cm. long, as thick as a little finger, straight or slightly bent, cicatricial in hardness and projecting into the duodenum. The hypertrophy is due to increase in mass of the individual fibers (Tanaka); the other layers show no histological changes. The mucosa is folded longitudinally and thus secondarily narrows the lumen." Especially noteworthy in the description is the statement that the tumor invaginates to a certain extent into the duodenum, and this is confirmed by Robertson, who regards partial invagination as reliable gross evidence of the condition.

Roentgenologic Manifestations

Excepting occasional reports of cases,[1,6] or mention in the differential diagnosis of

pyloric lesions,[2,8] hypertrophy of the pyloric muscle of adults has received scant attention in roentgenologic literature, probably because the condition was considered extremely rare, and because, from the roentgenologic standpoint, there seemed to be little to describe other than elongation and narrowing of the pyloric canal, together with evidences of obstruction in varying degree. On close study of the cases in our series, however, other and more interesting features became apparent.

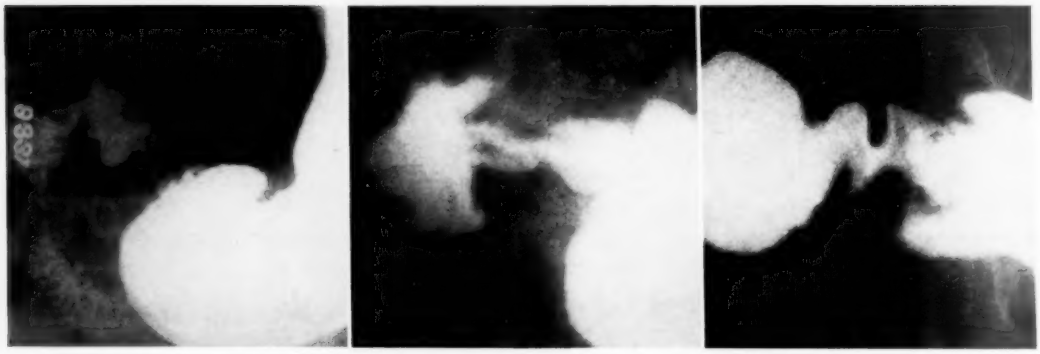
Lengthening of the pyloric canal occurs in practically every case. Normally, the canal does not exceed 0.8 to 1.0 cm. in length. When the muscle is hypertrophied the canal attains a length of from 2 to 4 cm., although the latter extreme is exceptional. If the elongation is moderate, the canal pursues a straight course, but if the lengthening is unusually marked, the canal curves upward toward the bulb. It might be anticipated that the channel would be constantly and extremely narrowed, but this is not the rule (Figs. 1, 2 and 3). Its diameter varies with the degree of physiologic contraction at the moment of view, but in relaxation the narrowing is seldom extreme, even when the hypertrophy is excessive. Often the axis of the canal is eccentric in relation to the antrum, and lies nearer to the lesser curvature than to the greater curvature (Fig. 2, *a*). The canal is not uniform in caliber. At the antral end the opening may be wide and have straight sides, or the tumefied muscle may project convexly into the antrum and form rounded shoulders about the aperture. Near the midpoint of the lower border of the canal, a narrow crevice or a larger, rounded depression is seen in many cases (Fig. 2, *a*). It is likely that the depression represents a folding of the mucosa produced by the upward bending of the canal. It may be misinterpreted as the crater of an ulcer, but, unlike a true niche, it will not retain barium when manipulated. According to Kaufmann's description of the morbid anatomy, the mucosal relief of the canal should often present longitudinal folds. Occasionally we have observed such folds, but in most cases the patterns were delicate, irregular, and variable. Not rarely the antral mucosa proximal to the tumor is wrinkled and contains deep, transverse sulci (Fig. 1, *c*).

Rarely, if ever, is the enlarged muscle palpable as a definite mass corresponding to the pyloric defect, but rather constantly in thin persons it slips away under the pressure of the examiner's fingers and gives the impression that the walls of the segment are merely rigid or perhaps infiltrated.

Hyperperistalsis, with an increase in the depth and number of waves visible at the

a *b* *c*

Fig. 2. Three cases of simple pyloric hypertrophy. In *a* the axis of the canal is eccentric, and a rounded depression midway on its lower border is evident. All three cases illustrate the partial invagination of the bulbar base, producing a mushroom form of the bulb.

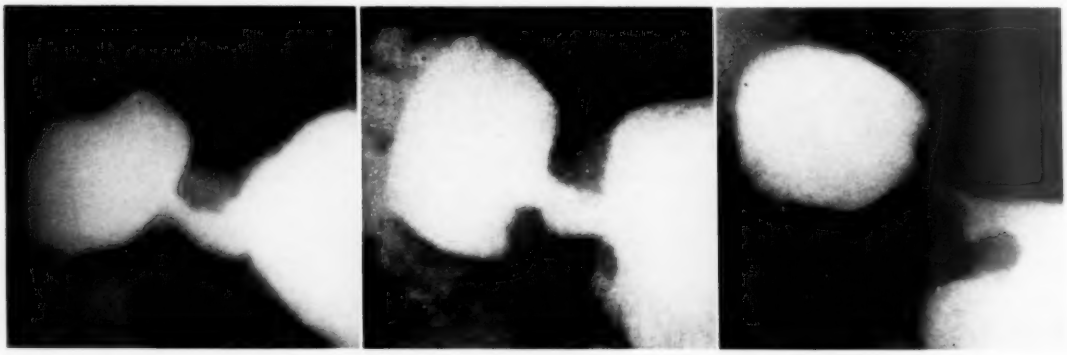


a *b* *c*

Fig. 3. Three cases of pyloric hypertrophy associated with gastric or duodenal lesions; in *a* with duodenitis; in *b* with gastric ulcer on the lesser curvature at the angle; in *c* with a prepyloric ulcer and a second small ulcer on the lesser curvature near the angle.

same moment, is an occasional observation. In the uncomplicated cases it is doubtless compensatory to obstruction. But, contrary to reasonable assumption, obstruction sufficient to produce retention of the barium meal after six hours is found in relatively few cases not associated with gastric or duodenal ulcer. This is true also of dilatation of the stomach, which is seldom encountered, although such dilatation results almost constantly from congenital hypertrophic stenosis of infants. It should be unnecessary to point out that hyperperistalsis, retention, and dilatation are common in cases of pyloric hypertrophy associated with duodenal or gastric ulcer.

Among all the manifestations of pyloric hypertrophy thus far described, none is absolutely characteristic of pyloric hypertrophy. As the pyloric deformity is persistent, unchanging in configuration, and resists antispasmodic drugs, reflex spasm from extrinsic causes can be excluded. But none of the signs, singly or in combination, will distinguish hypertrophy of the pyloric muscle from simple antral spasm (Fig. 4, *a*), from prepyloric ulcer with spasm (Fig. 4, *b*), from early scirrhous carcinoma (Fig. 4, *c*) or from gastric syphilis. This is well shown by the diagnoses returned in our series collected over five years. Among the uncomplicated cases there were exceedingly few in which a diagnosis of pyloric hypertrophy was made or mentioned as an



a *b* *c*

Fig. 4. Three cases of prepyloric narrowing from causes other than hypertrophy of the pyloric muscle. All lack the incurvation of the bulbar floor characteristic of pyloric hypertrophy; *a*, localized edematous gastritis with prepyloric spasm; *b*, prepyloric ulcer with spasm; *c*, early scirrhous carcinoma at the pylorus.

alternative. In several cases the examiner conservatively reported the existence of a lesion at the gastric outlet, without further specification; in the remainder he attributed the deformity variously to gastric or duodenal ulcer, or carcinoma. In the numerous cases associated with peptic ulcer the ulcer was usually discovered, but the pyloric contracture was evidently attributed to reflex spasm.

In several cases of pyloric hypertrophy in which examination has been made at the clinic in the current year we noted that the base of the duodenal bulb was concave, the concavity evidently being produced by partial invagination of the hypertrophied muscle into the bulb (Figs. 1, 2 and 3). The indentation usually appeared spontaneously at roentgenoscopic examination with the patient erect, but if absent or slight it could be elicited or made more pronounced by pressing the pyloric end of the stomach against the bulb. Roentgenograms made with the patient recumbent always showed the crescentic indentation if the bulbar base was adequately depicted and if the angle of roentgenography was at all appropriate. The roentgenograms in the series of cases collected over the period of five years were then reviewed. In all of those in which the bulbar base was fairly portrayed the indentation was evident. It varied in emphasis and sometimes in configuration. More often it swept, in a single continuous curve, across the base (Figs. 1, 2 and 3), but occasionally the curve was double, with an arch on either side of the pyloric canal (Fig. 3, *a* and *b*). In either case the mushroom shape of the bulb was striking (Fig. 2).

We have not observed any similar indentation in any case of reflex antral spasm, early carcinoma, early syphilis, or ulcer with pyloric spasm (Fig. 4). Further, the sign has substantial confirmation in the pathologist's statement that the elongated pyloric tube projects into the duodenum. Spasm, ulcer, and scirrhous carcinoma tend to produce shortening rather than elongation of the pyloric end of the stomach. For these reasons, although we cannot as yet affirm that the sign is strictly pathognomonic or invariably present, we feel that it is sufficiently distinctive, and that it occurs sufficiently often to be valuable in the diagnosis of pyloric hypertrophy.

SUMMARY

Hypertrophy of the pyloric muscle of adults, although not common, occurs often enough to require habitual consideration in the roentgenologic differential diagnosis of most pyloric lesions. At The Mayo Clinic, during the five years from 1927 to 1931 inclusive, 81 patients were examined by means of roentgen rays and presence of the condition was confirmed at operation. The cause of the hypertrophy has not been established definitely, but it is generally attributed either to persistence of congenital hypertrophic stenosis or to prolonged pyloric spasm. It is significant that among the 81 cases seen at the clinic, 51 were associated with peptic ulcer, duodenitis, chronic cholecystitis, or chronic appendicitis, all of which are frequently accompanied by pyloric spasm.

The most obvious direct roentgenologic manifestation of uncomplicated pyloric hypertrophy is elongation of the pyloric ring. A definite mass corresponding to the defect cannot be felt. Hyperperistalsis is observed occasionally; gastric dilatation and retention of residues from the six-hour meal are rare. None of these signs is characteristic of hypertrophic stenosis, for similar manifestations are seen often in early scirrhous carcinoma, early syphilis, and prepyloric ulcer with spasm.

Recently we have noted in cases of pyloric hypertrophy a crescentic indentation of the bulbar base. It was evident in all cases of a series collected over a period of five years, in which the bulbar base was plainly depicted, it accords with the morbid anatomy of hypertrophic stenosis, and it has not been observed by us in other states, either of health or disease. We believe, therefore, that this sign, in conjunction with prepyloric narrowing, will prove to be pathognomonic.

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DISCUSSION

Dr. G. W. Grier, Pittsburgh, Pa. Dr. Kirklin has done a great service to this Society by presenting this subject. Certainly until he presented his paper I had no idea this condition was so common. Sixty-five cases in a period of five years in one clinic is certainly enough cases to warrant our giving this subject considerable attention.

This condition, of course, has been known for a number of years, and has been attributed to a hangover from the so-called congenital pyloric stenosis. Personally I doubt that hypothesis as to the etiology of this disease, and I question whether the cases which occur in conjunction with other organic lesions are the same thing as the typical case of hypertrophy of the pyloric muscle. I doubt whether the generally recognized pylorospasm plays much part in the development of this disease. When we think of the thousands of cases of pylorospasm which are seen in the aggregate by roentgenologists over a period of a year, it would seem that if pylorospasm plays much part in the production of this particular and peculiar condition this would have been called to our attention long before this, and very often. As a matter of fact, in the one patient whom I have seen I don't think there was any spasm, and I don't think there was much spasm in the cases that Dr. Kirklin has shown, at least not spasm as I recognize it. In pylorospasm the pylorus is more or less shut in the presence of adequate or hyperperistalsis. In this case the pyloric canal was well filled, so that I doubt whether spasm has very much to do with the production of this condition.

The most important thing of all is, How do we recognize this condition? The one case that I have seen I diagnosed as annular carcinoma of the pylorus, and most of us here would have done the same thing.

I wish I thought Dr. Kirklin's new sign would help a great deal. Certainly in the case I saw I don't think it was present. I wish he would tell us whether there was anything in the clinical side of these cases which would help in the diagnosis, that is, with regard to the gastric analysis or anything else in the clinical record which would differentiate this condition from carcinoma, because it seems to me that is the most important lesson to be learned from this study. The one case that I saw did have considerable six-hour retention.

(Dr. Grier showed several slides.)

Dr. Kirklin (closing). Although only one case in this series was recognized roentgenologically as hypertrophied pyloric muscle before operation, it is our opinion after reviewing the 81 cases that the sign described will prove very helpful in recognizing such conditions in the future. The elongated pyloric canal in many of these cases is suggestive of malignancy, but as a rule malignancy does not produce the crescentic deformity at the base of the duodenal bulb.

Dr. George E. Pfahler, Philadelphia. How many cases have you had in all?

Dr. Kirklin. Eighty-one cases that we reviewed in the five-year period, in which the patients had been examined roentgenologically.

Dr. Pfahler. What number of stomach cases?

Dr. Kirklin. Examined roentgenologically?

Dr. Pfahler. Yes.

Dr. Kirklin. Approximately 60,000.

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BEHAVIOR OF THE HORMONE OF THE ANTERIOR HYPOPHYSIS IN A CASE OF TERATOMA TESTIS*

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THE sex hormone of the anterior hypophysis has been the subject of an investigation in this hospital during the past year. The hormone is excreted regularly in the urine of patients suffering from teratoma testis. The elimination of the hormone in these cases during and after treatment by roentgen rays and radium varies according to certain factors. These factors are as follows:

1. The embryonal character of the tumor.
2. The extent of the disease.
3. The radiosensitivity of the tumor.

The influence of each factor has been observed repeatedly in a study of 75 cases of teratoma testis requiring the completion of 700 biological tests of the urine. Since this material is too extensive to report in the time available, I have selected a single case which illustrates the features above mentioned.

CASE REPORT

N. D., aged thirty; admitted to the Memorial Hospital December 16, 1930. On admission the patient stated that his difficulties began six years ago with lumbar pain, especially on the left side. In August, 1930, he noticed a swelling in the left testicle which in October had reached the size of a fist. On October 24, 1930, the left testis was removed at a hospital in Brooklyn. The patient had lost 47 pounds during the year. Just before admission the patient noted enlarged nodes in the right axilla and a soft swelling of the right breast. Examination on admission revealed the absence of the left testis but at the upper end of the operative scar there was a firm, irregular mass, 3×2 cm. in diameter, which was interpreted as recurrent tumor. The left supraclavicular node was enlarged and in the right axilla there was a mass of enlarged, firm nodes, about 2.5 cm. in diameter. The right breast was enlarged and soft, and a colostrum-like material could be easily expressed from the nipple. The abdomen contained a mass of indefinite outline occupying the left lumbar fossa. Rectal examination revealed no tumor but the prostate was soft and

FIG. 1. Positive Aschheim-Zondek reaction obtained with urine from patient N. D., December 18, 1930.

enlarged to about one and one-half times normal size. Both vesicles were also palpable but soft. Roentgen examination of the chest on December 8 revealed multiple, scattered, sharply defined areas of varying size throughout the lung parenchyma, but particularly on the right side, which were interpreted as metastases. A clinical diagnosis of teratoma testis, postoperative, metastatic, was made, and treatment by high voltage roentgen rays directed to the left

* From the Service of Dr. B. S. Barringer, Department of Urology, Memorial Hospital, New York City; with the aid of The James Fund. Read at the Seventeenth Annual Meeting, American Radium Society, New Orleans, La., May 9–10, 1932.

Fig. 2. Positive Aschheim-Zondek reaction obtained with extract of urine from patient N. D., December 18, 1930.

abdomen and to both pulmonary areas was begun on December 16, 1930.

On December 18 the morning specimen of urine was obtained and injected into immature female mice after the technique of Aschheim-Zondek. Post-mortem examination of the ovaries of these mice 100 hours later revealed the typical changes due to the presence of the sex hormone of the anterior hypophysis in the urine (Figs. 1 and 2). Examination of the tissue removed at operation showed the structure of embryonal carcinoma of teratoid origin, Grade 4, relatively radiosensitive (Fig. 3). There was no suggestion that the tumor had the structure of a chorionepithelioma. This point is of interest, as the hormone of the anterior hypophysis was found in a case of chorionepithelioma of the testis reported by Heidrich in September, 1930. He contended that the demonstration proved the biological identity of chorionepithelioma in the male and female. The present case, however, shows that the hormone is eliminated in large amount in embryonal carcinoma, an observation supported many times since.

Influence of Tumor Structure

The amount of hormone eliminated in cases of teratoma testis varies in direct proportion to the embryonal character of the tumor. In teratomas of more adult type the hormone output may be only 200 to 600 units per liter while in chorionepithelioma the output may exceed 50,000 units per liter. The average embryonal carcinoma with lymphoid stroma produces between 2000 and 3000 units per liter. The urine was repeatedly tested by the Aschheim-Zondek technique and in order to study the quantitative output more accurately, extracts of the urine were made and tested by the same technique.

Extent of Disease

As the roentgen treatment proceeded and most of the tumor-bearing areas had been exposed, we began to note a rather sharp drop in the amount of hormone excreted, until the 24th of April when less

Fig. 3. Primary tumor. Embryonal carcinoma of teratoid origin, left testis, patient N. D.

than 300 units per liter were excreted (Fig. 4). This date was two weeks after the completion of the roentgen treatment.

In cases where the disease is not as widespread as in the present instance, the hormone may disappear rapidly from the urine. When only a small primary tumor exists, a single exposure to high voltage roentgen rays may eliminate the hormone from the urine within twenty-four hours.

RADIOSENSITIVITY

Other factors being equal, the radiosensitivity of the tumor will determine the rate of fall in hormone excretion when the tumor-bearing area is irradiated. In the present instance, while marked regression was obtained in some of the metastatic lesions, the tumor on the whole proved to be too radioresistant to permit of cure. At no time during the course of treatment, in this case, was the hormone entirely absent from the urine. In cases where the tumor is more radiosensitive, the hormone will disappear entirely as the course of treatment nears completion. This effect is a reliable indication as to the clinical radiosensitivity of the tumor and is also a favorable prognostic sign.

Fig. 4. Negative reaction from urine of same case after completion of first cycle of roentgen treatment.

Fig. 5. Positive Aschheim-Zondek reaction due to recurrence, patient N. D., May 1, 1931.

RECURRENCE

Tests conducted weekly for the following three weeks showed a gradual increase in the amount of hormone excreted (Fig. 5). This was interpreted as representing an increase in the number and extent of the metastases. Clinical examination confirmed this fact. I believed at first that the excretion of even traces of the hormone was indicative of recurrence or metastasis. Cases clinically well for periods varying from one to fifteen years may, however, continue to show traces of the hormone in the urine for long periods after roentgen treatment. Hence, the test should be interpreted as in-

Fig. 6. Hypertrophy of the seminal vesicles with true epithelial hyperplasia due to the sex hormone of the anterior hypophysis. (Autopsy—patient N. D.)

dicating recurrence only when repeated examination reveals a constantly increasing elimination of the hormone in the urine, as in the present case. In my material I find that this interpretation is consistent and that increasing hormone production in the urine of a treated case of teratoma testis indicates recurrence whether it can be detected clinically at the time or not.

IRRADIATION OF THE PITUITARY

The increase in hormone excretion continued up to May 5 when the pituitary was subjected to three exposures by high voltage roentgen rays, delivering 80 per cent of a skin erythema dose to each portal. Urine obtained the morning following the last treatment to the hypophysis revealed a sudden drop in the hormone production to approximately 800 units per liter, whereas on the 1st of May 3000 units had been excreted. On May 21 the hormone excretion had again increased to more than 3000 units per liter and from that time on the patient's condition grew gradually worse and he died on July 19, 1931.

An autopsy was obtained and the various organs of the body extracted according to the Zondek technique in order to determine the hormone content of each organ. In addition, sections were made of all the organs of internal secretion as well as of the tumor, both in treated and untreated areas.

ASSOCIATED CHANGES IN GENITAL ORGANS

Changes produced in the genital organs and in some of the organs of internal secretion by the presence of the hormone in the blood stream are of special interest. One well-known modification of the Aschheim-Zondek test utilizes the immature male mouse as a test object. In the presence of large amounts of the hormone, the vesicles hypertrophy and there is true epithelial hy-

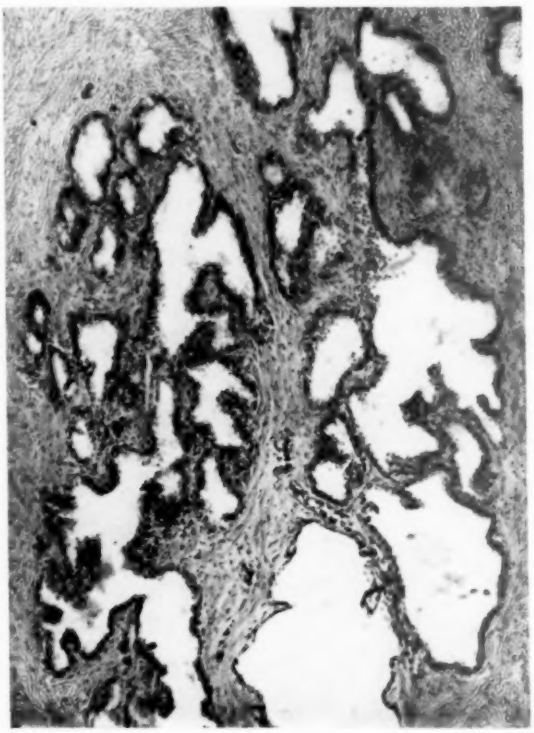

Fig. 7. Hypertrophy and epithelial hyperplasia of the prostate. (Autopsy—patient N. D.)

perplasia as well as marked congestion. Heidrich observed in his case of chorionepithelioma, in which hormone excretion just before death exceeded 50,000 units per liter, that there was a marked hypertrophy of the prostate and seminal vesicles. Sections of the organs at autopsy revealed a true epithelial hyperplasia in both of these structures. I have been able to confirm these observations both clinically and at post mortem in the present case, as well as in two others since that time (Figs. 6 and 7). At autopsy this enlargement is shown to be due in part to hyperemia and congestion and in part to true epithelial hyperplasia. The pituitary in the present case is indistinguishable, histologically, from the pituitary adenoma of pregnancy.

Another interesting feature is the marked hyperplasia of the cells of Leydig in the remaining testis of this individual (Fig. 8). This observation is confirmed by Heidrich, and by other post-mortem material in my possession.

SUMMARY

1. The excretion of the sex hormone of the anterior hypophysis in the urine of the male suffering from a testicular tumor indicates the presence of teratoma.

2. Irradiation directed at the primary tumor, and its metastases, produces a decrease in hormone elimination which is in proportion to the embryonal character of the tumor, the extent of the disease, and its radiosensitivity.

3. Recurrence after treatment is indicated by a constantly increasing elimination of the hormone in the urine whether the recurrence can be demonstrated clinically or not.

4. The hormone of the anterior hypophysis when excreted in large amount in men produces a soft swelling of the prostate and vesicles with true epithelial hyperplasia. The pituitary in such cases is indistinguishable from that of pregnancy and there is a concurrent hyperplasia in the interstitial cells of the testis.

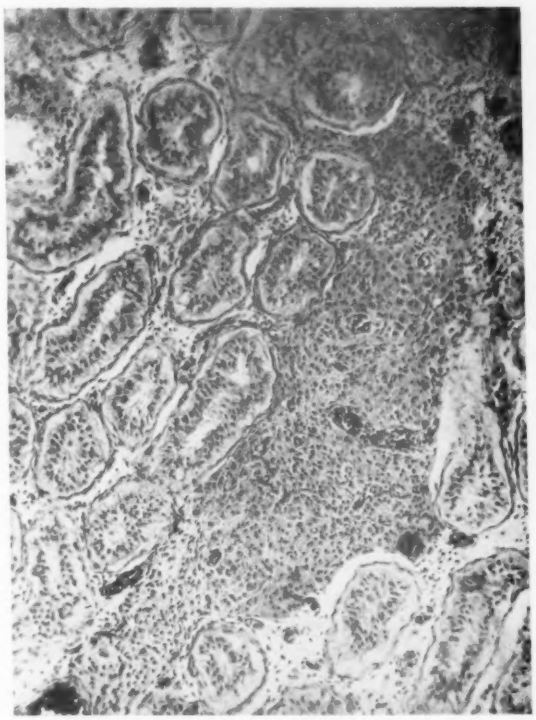

Fig. 8. Hyperplasia of Leydig's cells in the right testis. (Autopsy—patient N. D.)

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DISCUSSION

Dr. Burton J. Lee, New York City. The Memorial Hospital staff feels that this painstaking piece of research is one of the best that has come forth from the hospital in many years. Dr. Ferguson is to be congratulated, and also the Memorial Hospital, where the work was done.

Dr. Charles L. Martin, Dallas, Texas. This paper is very interesting because it shows a definite relationship between a radiosensitive tumor and the glands of internal secretion. Many observers have in the past assumed the existence of such a relationship on purely theoretical grounds. The marked improvement in certain bone metastases from cancer of the breast following the production of an artificial menopause offers a similar field for investigation. Let us hope that some other able investigator will follow Dr. Ferguson's example and unravel this problem.

I would like to ask the essayist whether he thinks the hormone that he obtains in his cases is elaborated in the tumor or in the pituitary gland and also whether he feels that roentgen therapy directed to the pituitary is of value in such patients.

Dr. Ferguson (closing). As to the source of the hormone. I am not prepared to answer. The hormone content of the tumor itself in some cases is greater than that of the urine, the blood, or the pituitary. In the absence of definite knowledge of the chemical structure of the hormone, it will take at least five years to answer the question through clinical and anatomical investigation.

With regard to treatment, I have been able to irradiate the pituitary in only three cases. The report of Voltz to the League of Nations is of interest in this connection. He has been treating carcinoma of the uterus since 1923 by irradiation of the pituitary prior to local treatment. His statement is that the general condition of the patient seemed to be improved by this technique. In the case here reported, a sharp drop in the hormone excretion was demonstrated following irradiation of the pituitary.

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ROENTGEN FINDINGS IN SPLENOMEGALY*

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THE relative accuracy of the gastrointestinal roentgen study for the determination of the various forms of intrinsic pathology of the stomach and intestines is, by this time, rather generally recognized among all clinicians. The value of the same examination in the differentiation of abdominal masses not representing intrinsic gastrointestinal pathology is much less commonly known, hence it has seemed worth while to analyze these 6 cases of splenomegaly in an effort to evaluate the gastrointestinal roentgen findings and show their considerable accuracy in differentiating splenic tumors from other upper abdominal masses such as pancreatic tumors, (left) renal tumors, (left lobe) liver tumors, and retroperitoneal tumors, with which there might be some clinical confusion.

ANATOMY

The changes from the normal in the gastrointestinal findings which an enlarged spleen will produce are due to the usual close approximation against its several surfaces of the splenic flexure of the colon, the stomach, the left kidney, and the diaphragm. There is still one additional surface of the spleen, namely, the pancreatic surface, upon which the tail of the pancreas lies. However, inasmuch as the normal pancreas never casts a primary shadow the close approximation of this structure to the spleen has not been found of any practical value in the roentgenologic recognition of splenic enlargements. On the other hand, the intimate relationships of the stomach, splenic flexure, and left kidney to the spleen are a matter of the greatest importance in recognizing splenic enlargements.

DIRECT EVIDENCE

At this point it might be emphasized that it is not believed that by observing these indirect signs of displacements of the stomach, splenic flexure, and left kidney, one will be able to recognize the very slightest abnormal splenic enlargements any more than one might similarly hope to recognize the slightest enlargements of the left auricle by displacement of the esophagus alone. A certain amount of work has been done in an effort to determine the normal variations in size and position of the spleen as studied roentgenologically, hence there is some value in making linear measurements of this organ, just as there is unquestioned value in roentgen measurements of the heart. A study of 1,200 liver and spleen roentgenograms of young adults at the University of California was made by Moody and Van Nuys.[7] They found that with the usual Potter-Bucky diaphragm technique the average length of the spleen was 12.9 cm. with, however, variations ranging from 7.0 to 16.0 cm., and the width of the spleen was approximately 6 cm. with variations from 3.5 to 10.0 cm. With such wide variations within normal limits it is obvious that minor changes in size could not be recognized even by roentgen mensuration except by serial film examination. Nevertheless the making of splenic measurements on the routine plain abdominal films prior to barium administration is distinctly worthwhile in all cases of splenic enlargement, since this constitutes *direct* evidence of splenic enlargement when measurements above the top limits of normal can be demonstrated. Plain films of good quality which include the left diaphragm outline usually afford an accurate length measurment and not infrequently also a reasonably accurate thickness measurement, the latter being at times facilitated by injecting air into the colon, and in other cases by measuring to the lateral margin of the dis-

* From the X-ray Departments, St. Luke's and Marquette Hospitals and the A. O. Smith Corporation, Department of Preventive Medicine, Milwaukee, Wis. Read before the Roentgen Section, Wisconsin State Medical Society, Madison, Wis., May 27–28, 1932.

placed large or small intestine. In this series of cases all measurements obtainable were considerably above the top limits of normal, the spleen lengths varying from one and one-half to two and one-third times the normal average.

INDIRECT EVIDENCE

It must not be inferred that every *palpable* spleen will show the gastrointestinal roentgen findings to be described as having taken place in the present series of 6 cases. However, in frank splenic enlargements such as occur in the leucemias, Banti's disease, Gaucher's disease, Hodgkin's disease, etc., it is believed that the findings described as characteristic would be present in greater or lesser degree and in one of the cases here reported a considerable enlargement of the spleen was demonstrable, the roentgen picture being characteristic. Yet neither before nor after the findings were known was it possible to palpate the enlarged spleen.

In an analysis of the 6 cases here reported the most characteristic and constant change observed during the gastrointestinal study was the downward and inward displacement of the splenic flexure. While very variable positions of the hepatic and splenic flexures are found during routine gastrointestinal studies and while great variations are now accepted as being of no clinical importance, in most instances at least, it is extremely rare to find the splenic (left colic) flexure at a lower level in the abdomen than the hepatic (right colic) flexure, except in cases of situs inversus or in the rather infrequent case where there is a wide space intervening between the lower pole of spleen and the splenic flexure. Most anatomists, including Gray,[5] Piersol,[8] Cunningham,[3] and Eycleshymer and Jones,[4] do not describe the wide variations in relationship between lower pole of spleen and splenic flexure of colon which can be readily observed if looked for in every day roentgenologic practice. While in a large percentage of cases the splenic flexure will be found roentgenologically to lie in close proximity to the inferior (colic) surface of the spleen (Fig. 1*a*), it is not a rarity to find the splenic flexure held in close proximity to the under surface of the left diaphragm (at least 8 to 10 cm. above the "anatomical position") not only in the horizontal but also in the vertical position, this position suggesting an unusually short phrenico-colic ligament (Fig. 1*b*). Less frequently the opposite extreme is seen and the flexure will be found to lie 5 to 10 cm. below the lower pole of the spleen instead of in close proximity to its lower pole, this position suggesting an unusually long or absent phrenico-colic ligament (Fig. 1*c*). However, this latter position is relatively quite uncommon, hence this finding of a low splenic flexure should at once suggest the possibility of splenic enlargement.

The changes from the normal in the position and appearance of the stomach were somewhat more variable. In several instances the enlarged spleen produced only a compression of the posterior wall of the upper end of the stomach with little or no right lateral displacement, while in several of the larger spleens there was a rather remarkable displacement of the cardiac end of the stomach to the right, this being of such a degree in two instances as to even affect slightly the position of the lower third of the esophagus. In one instance the deformity produced in the stomach contour, by the splenic tumor, was such as to arouse suspicion of possible coexistent second lesion such as retroperitoneal glandular enlargement because of the peculiar serrated indentation produced by the nodular spleen upon the upper posterior part of the stomach. Hence, while in most instances the compression or displacement will result in a relatively smooth gastric outline, it may produce a somewhat irregular contour, though not of the same appearance as that produced by intrinsic lesion of the upper end of the stomach such as carcinoma. The variability of the gastric findings seems in some measure, although not exactly, proportionate to the degree of splenic enlargement, those several spleens appearing

largest by roentgen ray showing the most marked displacement of the stomach to the right. It would seem that the enlarged spleen must embrace the upper end of the stomach in rather variable manner so that in some cases the upper end of the stomach is only pushed forward, while in others the enlarging spleen embraces the greater curvature aspect of the cardiac end of the stomach and pushes the upper portion of the stomach markedly to the right. The morphology of the upper end of the stomach must also be a factor.

Holmes[6] states that upward displacement of the left side of the diaphragm should make one consider the possibility of splenic enlargement. Piersol states that when the spleen is greatly enlarged at any age of life there is apt to be upward displacement of the diaphragm. That upward displacement occurs at times is indicated by the case of echinococcus cyst of the spleen described by Wessler and Jaches.[10] However, in this series of cases it did not occur in any instance. Persistence in a normal position of the closely overlying left diaphragm would seem essential to the regular occurrence of displacement of the nearby intra-abdominal organs. This it would seem from analysis of these cases is probably the rule since the spleens here discussed represent huge enlargements, both cystic and solid.

Butler and Ritvo[2] emphasize displacement of splenic flexure and stomach and state that splenic enlargements usually cause typical pressure deformities and displacements of these two structures.

1*a* 1*b* 1*c*

Fig. 1*a*. Splenic flexure in "textbook normal" position with reference to spleen, it being in close proximity to the inferior pole and colic surface.

Fig. 1*b*. Note unusually high position of gas-containing splenic flexure which is in close proximity to under surface of diaphragm. This position of the splenic flexure is more frequently encountered than the opposite extreme where the splenic flexure lies at a lower level than the hepatic flexure and well below the colic surface of the spleen.

Fig. 1*c*. Unusually low splenic flexure with wide space intervening between splenic flexure and colic surface of spleen. This position suggests an unusually long phrenico-colic ligament.

When the spleen is considerably enlarged, because of its rather close approximation to the upper pole of the left kidney, a greater or lesser degree of downward displacement of the left kidney would be expected to occur. Such a displacement was well demonstrated in 2 of the cases here shown where the gastrointestinal roentgen findings were not looked upon as conclusive evidence of splenic tumor or where renal

tumor was clinically suspected, although renal displacement, like stomach displacement, is not a constant finding.

DIFFERENTIAL ROENTGEN DIAGNOSIS

As already indicated, splenic tumors require differentiation clinically from left renal, pancreatic, left lobe hepatic, retroperitoneal glandular, fluid accumulations in the lesser peritoneal cavity, and intrinsic gastric or splenic flexure tumors.

Renal tumors ordinarily produce no displacement of any kind of the splenic flexure and the compression of the stomach from behind which a large renal tumor at times produces is well down against the fundus portion of the stomach so that the cardiac end remains in a normal position.

Pancreatic tumors give very variable roentgen findings, those of the tail portion lying in the left abdomen, producing, according to Butler and Ritvo, a smooth, rounded, compression deformity on the lower portion and greater curvature side of the stomach, although at times if the growth extends a considerable distance into the lesser peritoneal cavity there may be a flattening on the lesser curvature side with narrowing of the media and antrum. The jejunal loops may be displaced downward and to the side while the splenic flexure if displaced will go to the left. Tumors arising from the head of the pancreas are not ordinarily confused with splenic tumors but would require differentiation more from intrinsic tumors at the lower end of the stomach, also liver or gallbladder tumors, because of the deformities and displacements of the pyloric end of the stomach and duodenal loop.

Tumors arising from the left lobe of the liver are not often encountered. One case of a cyst arising from the fissure between the right and left lobes which was the size of a small orange was recently personally observed. On gastrointestinal study the only evidence of its presence was a shallow concavity produced by it on the lesser curvature of the stomach in the region of the incisura angularis. Tumors of appreciable size originating in the left lobe, or diffuse enlargements of this lobe would, according to Brown,[1] press upon the *anterior* surface of the stomach and, if sufficiently large, displace the upper part of the stomach *backward*. The splenic flexure would ordinarily show no change from the normal position.

Retroperitoneal glandular enlargements, whether in the nature of primary or metastatic tumors, often reach marked size and because of their position near the midline are, of course, readily palpable. However, upon gastrointestinal examination they produce little or no recognizable displacement other than some pressure deformity on the posterior wall of the stomach usually well away from the cardiac end, together with at times some demonstrable separation of the filled loops of small intestine, if serial observations be made during the first four hours of the gastrointestinal study.

A case of fluid accumulation in the lesser omental cavity was reported recently which, on gastrointestinal study, showed the splenic flexure displaced downward but the stomach was displaced downward and to the left (origin of fluid accumulation was a ruptured malignant ulcer on the lesser curvature of the stomach). Very recently a case was reported of a large tumor in the left hypochondrium which was thought clinically to be an enlarged spleen but which, on gastrointestinal study, showed a large niche on the lesser curvature of the stomach, several inches above the pylorus, interpreted as representing a subacute perforating gastric ulcer which, upon exploratory laparotomy, and subsequently upon necropsy examination, was proved due to a leiomyosarcoma, arising from the posterior wall of the stomach which had undergone necrosis and perforation with a walled-off abscess in the lesser peritoneal sac, and the spleen was found to be normal in size.[9]

Intrinsic tumors of the cardiac end of the stomach or of the splenic flexure of the colon are ordinarily not associated with

any displacement of either of these structures and the fact that the tumor is intrinsic is usually rather definitely determinable from the gastrointestinal and barium enema examinations.

CASE REPORTS

Case 1 (*Chronic lymphatic leucemia*). Mrs. M.K. (referred by Dr. John Huston), aged sixty-six, a widow, was first seen September 30, 1929, at which time her chief complaint was pain and weakness in the knees. She stated that she was so weak that she was only able to walk a very short distance after which she would have to sit down. Nine months ago her weight was 185 pounds, present weight, 140 pounds.

Physical examination showed a rather aged woman who appeared definitely anemic and with a peculiar icteric tint to the skin. Examination of the abdomen showed a large spleen reaching a little distance to the right of the midline and down below the level of the iliac crest. The liver was palpable. The only superficial gland enlargement was in the left axilla. Examination of the blood showed red cells 2,100,000, white cells 144,000, hemoglobin 43 per cent, small lymphocytes 89 per cent, large lymphocytes 10 per cent, polymorphonuclears 1 per cent. The stained cells showed considerable deformity with moderate polychromatophilia. The clinical diagnosis was chronic lymphatic leucemia.

Roentgen examination revealed both kidneys clearly on the plain film examination and showed *no* downward or inward displacement of the left kidney, in this instance the kidney maintaining its normal position despite the huge splenic enlargement (Fig. 2*a*). During gastrointestinal study the stomach was seen to be displaced to the right (Fig. 2*b*), and the splenic flexure was displaced downward to a level somewhat below the position of the hepatic flexure (Fig. 2*c*). Roentgenographic measurements of the spleen (films taken with Potter-Bucky diaphragm) were: length 26.0 cm., width 11.5 cm.

2*a* 2*b* 2*c*

Fig. 2*a*. Case 1. Splenomegaly associated with lymphatic leucemia. Lower pole of spleen reaches just below level of iliac crest but produces *no* displacement of left kidney.

Fig. 2*b*. Case 1. Patient in anteroposterior horizontal position. Cardiac end of stomach is displaced downward and toward the right.

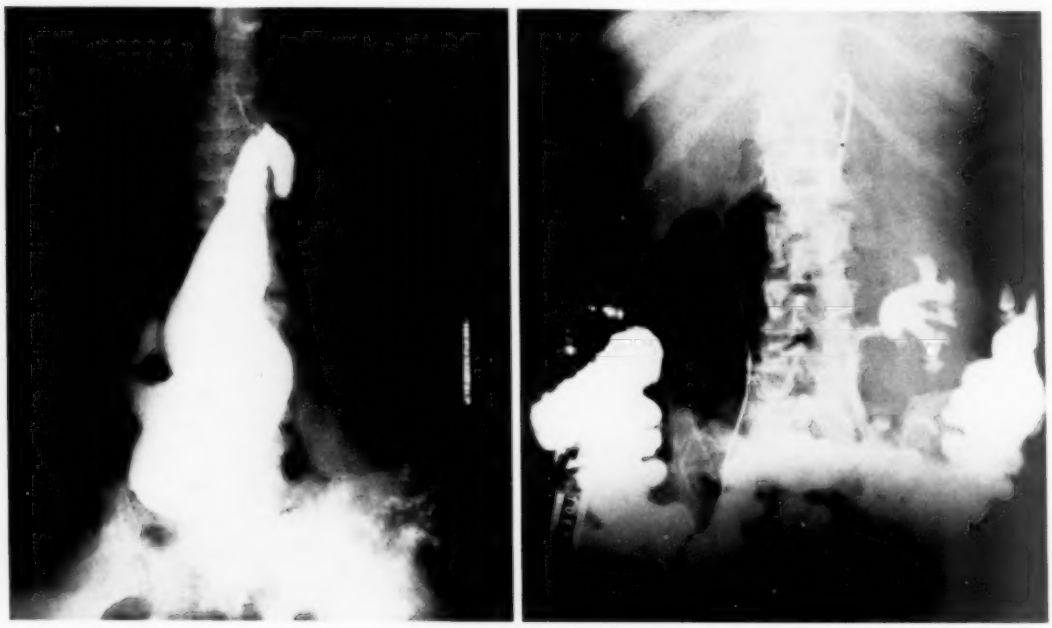
Fig. 2*c*. Case 1. Five-hour roentgenogram showing splenic flexure displaced downward below level of hepatic flexure.

Course. Roentgen treatments were given over both the spleen and the long bones beginning October 4, 1929, and the first series terminating November 19 at which latter date examination of the blood showed red cells 2,700,000, white cells 3,300, hemoglobin 50 per cent, small lymphocytes 65 per cent, large mononuclears 9 per cent, polymorphonuclears 29 per cent. The patient's general condition had improved mark-

edly so that she was able to walk a considerable distance without tiring and was no longer complaining of the distress in the legs. The spleen was considerably decreased in size, though still easily palpable. The patient continued to do well under intermittent roentgen irradiation for a period of six months during which time she continued to feel quite well and took an active interest in her affairs, up to a matter of several days before her death which was in the nature of a cardiac failure.

of the abdomen showed no distention or rigidity, but a large palpable tumor was present in the left upper abdomen extending down as far as the level of the umbilicus. Urinalysis was essentially negative on two examinations. Examination of the blood showed 3,800,000 red cells, 3,300 white cells, hemoglobin 60 per cent, polymorphonuclears 75 per cent, small lymphocytes 22 per cent, large lymphocytes 2 per cent.

Roentgen examination of the chest was essentially negative. The gastrointestinal tract



3*a* 3*b*

FIG. 3*a*. Case II. Splenomegaly occurring in Banti's disease. Anteroposterior roentgenogram of stomach showing marked displacement of stomach downward and to right with nodular indentation on posterior wall and greater curvature producing a diverticulum-like recess at the cardiac end.

FIG 3*b*. Case II. Anteroposterior roentgenogram showing left kidney displaced downward to level of hepatic flexure.

CASE II (*Banti's disease*). Mrs. T.W. (referred by Dr. Henry Gramling), aged sixty-two, married, admitted to St. Luke's Hospital June 22, 1930, complaining of sharp pain in the left side which seemed to interfere considerably with eating during the past week. Over an interval of the past preceding several months, prior to admission to hospital, there had been a considerable loss of weight so that malignancy was rather strongly suspected.

Physical examination revealed an elderly woman, not acutely ill. Head, neck and chest findings were essentially negative. Examination

showed a marked displacement of the stomach to the right and forward with a rather peculiar contour to the greater curvature and posterior wall of the displaced stomach, there being a finger-like projection of the barium shadow at the cardiac end which at first suggested a diverticulum but was finally considered to be more probably merely a recess formed as a result of the extra-gastric pressure (Fig. 3*a*), there being no definite stasis in this portion of the stomach at five hours. The examination of the colon showed the entire colon to be rather low, the splenic flexure being displaced some-

what downward but with no inward displacement. Because of the somewhat atypical roentgen findings as concerned the appearance of the stomach and splenic flexure, pyelographic examination of the left side was recommended. This examination revealed a normal pyeloureterogram except for downward displacement of the left kidney, the pelvis of which was opposite the 4th lumbar vertebra (Fig. 3*b*). The final impression was that the spleen must be enlarged but that a second pathological process might coexist retroperitoneally because of the peculiar nodular indentation of the stomach. Roentgenographic measurements of the spleen on the plain Potter-Bucky films were: length 26.6 cm., width not accurately obtainable.

Course. Operation revealed a large nodular spleen which was removed, with some difficulty, by Dr. Gramling. The spleen weighed 3 pounds, measured 8×6×4 inches and was described by the pathologist, Dr. E. L. Tharinger, as being consistent with Banti's disease, dissection showing only a marked increase of the pulp. There were no other characteristic changes.

Case III (*Hodgkin's disease*). Miss R.R. (referred by Dr. Fred Stratton), aged twenty, unmarried, admitted to Marquette Hospital May 9, 1928, with complaint of chills and fever for the past week. In 1924 she first noticed swelling of the posterior cervical glands on the right side. These were hard but painless and were submitted to surgical removal the same year. Shortly thereafter swelling developed in the anterior cervical glands and these were removed in 1926 at the time of a tonsillectomy. Pathological examination by Dr. Edward Miloslavich revealed the glandular enlargement to be of the Hodgkin's type. At the time of admission to the hospital she also complained of a chronic cough with slight expectoration and stated that she had lost 10 pounds in the past two months.

Physical examination revealed a fairly well developed and nourished young woman, not acutely ill. The examination of the head and neck was essentially negative except for the postoperative scars on the right side. The heart and lungs were likewise negative on physical examination. Examination of the abdomen showed a hard mass the size of a large orange reaching downward below the left costal margin, with several smaller masses. The liver could not be palpated. Examination of the blood showed red cells 3,800,000, white cells 4,200, hemoglobin 65 per cent, polymorphonuclears 89 per cent, small lymphocytes 10 per cent, transitionals 1 per cent, platelet count 370,000. Urinalysis negative. During the patient's stay of two weeks in the hospital she ran a septic temperature, the maximum being 103° F. with the pulse rate varying from 110 to 140.

Roentgen examination of the chest revealed no evidence of mediastinal glandular involvement or pathology in the heart or lungs. The preliminary film of the abdomen showed no primary shadow of a tumor mass but the left kidney outline was obscured. The gastrointestinal examination showed a large hypotonic stomach with extrinsic pressure filling defect on the posterior wall, the mass being definitely located in back of the stomach (Fig. 4*a*). By barium meal examination the gas-filled splenic flexure was found to be displaced downward to a slightly lower level than the hepatic flexure (Fig. 4*b*), although when a barium enema was given the distended splenic flexure rose to a slightly higher level than the hepatic. Roentgenographic measurements of the spleen (plain films) were: length 20.0 cm., width not obtainable. The roentgen findings were those of a large spleen, the extrinsic filling defect along the posterior wall of the stomach being very possibly produced by retroperitoneal glands.

The clinical diagnosis was Hodgkin's disease with abdominal involvement.

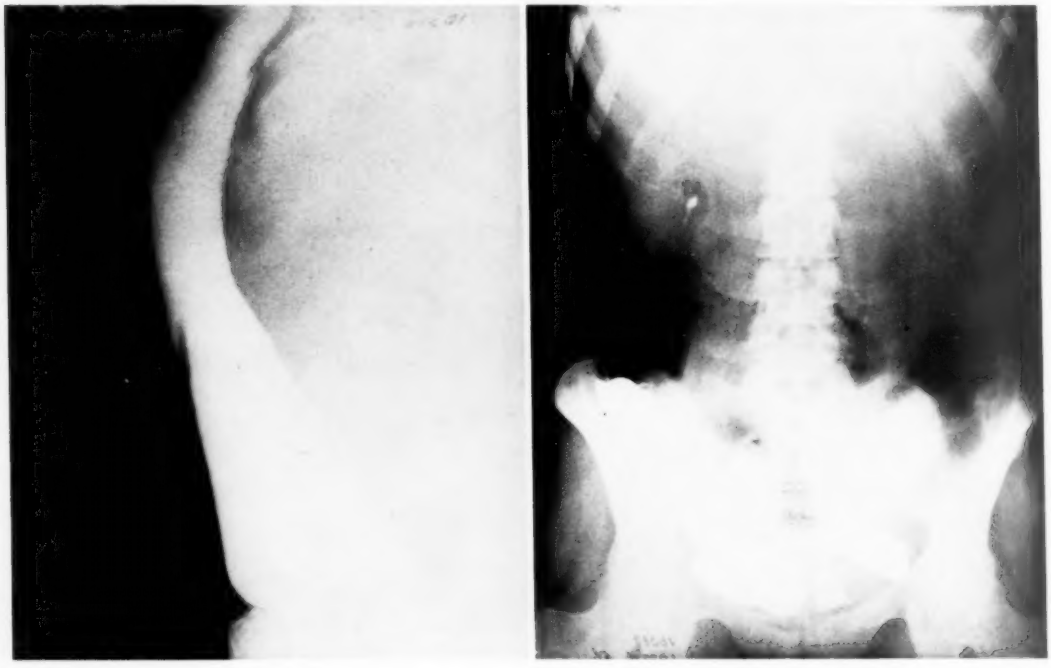
Course. Roentgen treatments were given beginning June 13, the second treatment being given June 16 and the third July 16, in each instance the portal being the left upper quadrant anteriorly. When examined at the time of the third treatment the general appearance of the patient had improved markedly, she had gained 15 pounds in one month, showed improvement of color, and the tumor mass had almost entirely disappeared; the tendency to gastric upsets, which was present just prior to beginning treatments, had likewise disappeared.

Case IV (*Traumatic splenomegaly?*). Mr. J.S. (referred by Dr. Chester Echols), aged thirty-four, married, a laborer, was admitted to St. Luke's Hospital May 16, 1930, with a complaint of intermittent pains low down in the abdomen which had been present since being struck in the left flank by a shovel about ten months prior to admission to the hospital. He was treated immediately after the injury for suspected perforation but was not operated

upon. The past history was essentially negative; he had always been in good health and regularly at work.

Physical examination revealed a well developed and nourished young male who showed at the time of physical examination some evidence of abdominal distress. The examination of the head, neck, and chest was essentially negative. Examination of the abdomen showed considerable rigidity with multiple areas of tenderness but no definitely palpable masses. Urinalysis was negative on two examinations. Blood examination revealed red cells 5,600,000, white cells 8,500, hemoglobin 85 per cent, polymorphonuclears 85 per cent, small lymphocytes 15 per cent. Roentgen examination of the gastrointestinal tract was requested in an effort to show some evidence of partial obstruction.

Roentgen examination of the gastrointestinal tract revealed, in this instance, no definite displacement of the stomach, either to the right or anteriorly; however, studies of the colon showed a downward and inward displacement of the splenic flexure, the proximal descending colon being displaced inward a considerable distance (Fig. 5) although on filling of the colon with the barium enema the distended splenic flexure passed upward and over the enlarged spleen to a fairly normal level in the upper abdomen. Roentgenographic measurements of the spleen (films made with Potter-Bucky diaphragm) were: length 20.0 cm., width 11.5 cm. There was no evidence of kinking, adhesions, or other pathology of this nature demonstrable, the only definite roentgen finding being the evidence of a greatly enlarged spleen.



4*a* 4*b*

Fig. 4*a*. Case III. Splenomegaly associated with Hodgkin's disease. Right lateral roentgenogram of stomach reveals marked compression of posterior wall of upper half of stomach. (Atypical case because of coexisting retroperitoneal gland masses.)

Fig. 4*b*. Case III. Five-hour roentgenogram showing gas-filled splenic flexure displaced downward to slightly lower level than hepatic flexure.

Course. Exploration by Dr. Echols revealed no evidence of adhesions involving any portion of the bowel but confirmed the roentgen impression of splenic enlargement, the spleen being estimated to be five times its normal size and symmetrically enlarged, firm in consistency, and with a mottled surface showing irregular, yellowish, coalescent patches. The sur-

face of the spleen was granular and was rough to the touch. The splenic veins were enormously enlarged and tortuous, but no nodules were palpated in the pedicle of the spleen. There were fibrous adhesions over the anterior and inner surfaces. The liver, kidneys, entire peritoneum, and intestine all appeared normal. A small biopsy specimen was removed which, on microscopic examination by Dr. E. L. Tharinger, showed a greatly thickened capsule, the splenic pulp showing thickening of the trabeculae and patches of fibrosis. The final diagnosis was chronic (traumatic ?) hypertrophic splenitis.

Case v (*Idiopathic splenomegaly*). Mr. A.W. (referred by Dr. T. L. Squier), aged fifty-five, married, a laborer, was examined October 31, 1930, at which time he had no complaint. The past history was essentially negative except for an attack, at the age of nineteen, of fever during which he was sick in bed for eighteen weeks.

Physical examination showed sibilant râles at both bases and the chest roentgenogram showed old pleural fibrosis at the left base. Physical examination of the abdomen was negative. Urinalysis was negative. Blood examination showed red cells 4,700,000, white cells 7,700, hemoglobin 83 per cent, polymorphonuclears 42 per cent, transitionals 2.5 per cent, small lymphocytes 55 per cent.

Fig. 5. Case iv. Splenomegaly, traumatic (?). Twenty-four-hour roentgenogram showing downward and inward displacement of splenic flexure. (No gastric displacement or compression could be demonstrated in this case; note normal position of gas bubble in cardiac end of stomach.)

Fig. 6. Case v. Splenomegaly associated with no clinical findings except lymphocytosis. Double meal posteroanterior roentgenogram taken at twenty-four hours showing splenic flexure displaced inward and slightly downward by long spleen with upper end of stomach displaced somewhat to right.

Roentgen examination of the gastrointestinal tract was made primarily to exclude latent malignancy, at which time a moderate displacement of the stomach to the right with slight displacement also of the lower esophagus was observed. Examination of the colon showed downward and inward displacement of the filled splenic flexure to the level of the hepatic flexure (Fig. 6). On this examination the outline of the lower pole of the spleen was well visualized, the tip of which reached nearly to the iliac crest. The roentgen findings were characteristic of well marked splenic enlargement, that is, there was not only displacement of splenic flexure and stomach, but the shadow of the enlarged spleen was clearly demonstrable so that roentgenographic mensuration was easily

done. Roentgen measurements (films made with Potter-Bucky diaphragm) were: length 25.0 cm., width 9.0 cm. Despite this, the spleen was not found palpable even on second abdominal palpation.

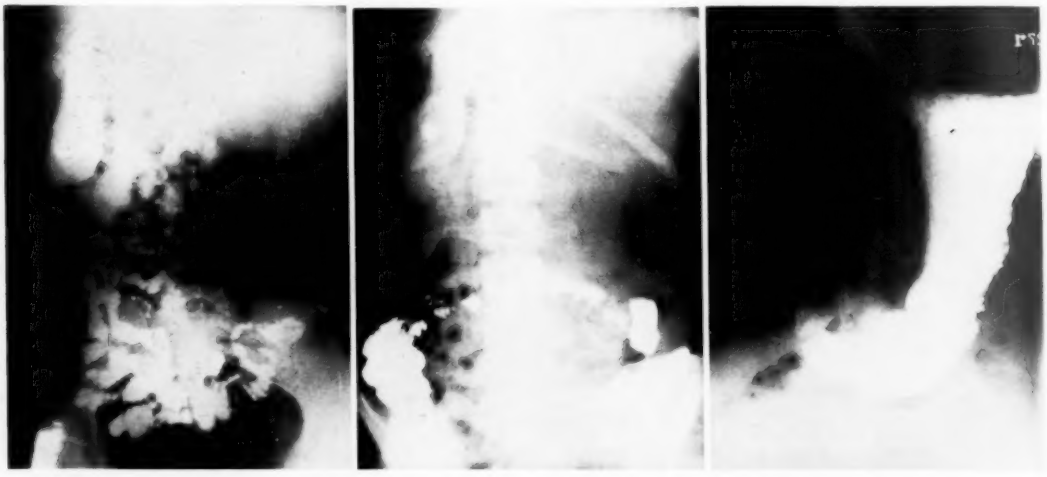
Course. Because of the entire absence of symptoms or other definite justification for active therapy, no treatment was advised, other than further observation of the spleen.

Case vi (*Splenic cyst*).* Mrs. C. M. (referred by Dr. Roy Benton), aged twenty-eight, housewife, was examined August 20, 1930, with a complaint of pulling in the left side, first noticed following pleurisy in 1926. A mass was noticed by the patient in the left upper abdomen which had shown considerable enlargement in size in the past six months.

Physical examination showed a large mass in the left side extending down to about two-finger breadths of the iliac crest with a soft area at the upper pole suggesting cystic degeneration, the remainder of the mass being firm and nodular. Blood examination showed red cells 4,500,000, white cells 8,100, hemoglobin 87 per cent, polymorphonuclears 64 per cent, small lymphocytes 34 per cent, large mononuclears 1 per cent, transitionals 1 per cent, platelets 170,000. No unusual cells were seen in the blood smear. The liver was not enlarged.

Roentgen examination following barium meal showed a marked displacement to the right, not only of the stomach, but also of the lower end of the esophagus (Fig. 7*a*). The study of the colon showed a marked downward and inward displacement of the splenic flexure (Fig. 7*b*). The roentgen findings were those of huge splenic tumor but there was much difference of clinical opinion even after the gastrointestinal studies. Roentgenographic measurements of the spleen on gastrointestinal films (Potter-Bucky diaphragm not used) were: length 29.0 cm., width not obtainable. With all the evidence summarized, the consensus of clinical opinion was against splenic tumor and favored pancreatic cyst or cystic kidney, although intravenous pyelographic studies showed a normal pyelogram on the right side with a marked downward and inward displacement of the kidney on the left, the pyelogram shadow being rather largely obscured because of its position overlying the 4th lumbar vertebra (Fig. 8*a*).

Course. Operation by Dr. Frank Darling re-



7*a* 7*b* 7*c*

Fig. 7*a*. Case vi. Splenomegaly associated with large cyst formation of upper pole of spleen. Anteroposterior roentgenogram showing stomach and duodenum lying entirely to right of midline with jejunum displaced downward and to right.

Fig. 7*b*. Case vi. Double meal film taken at twenty-four hours showing downward displacement of splenic flexure to level slightly below hepatic flexure.

Fig. 7*c*. Case vi. Postoperative roentgenogram of stomach with patient in erect position showing stomach lying in "textbook normal" position.

* This case is being reported in greater clinical detail elsewhere by Dr. Roy W. Benton.

vealed a large cystic mass presenting into the operative incision, into which a trocar was inserted and from which 2 quarts of chocolate fluid were removed. The cyst was explored and was found to be part of the spleen arising from the upper medial pole. The spleen was enlarged downward, the lower border being two-finger breadths above the iliac crest; it was densely adherent to stomach and pancreas but by careful dissection the adhesions were separated. The cyst wall was removed and the abdomen closed, and the patient made an uneventful recovery.

Postoperative roentgen studies revealed the stomach now to be "textbook normal" in form and position (Fig. 7*c*). The gas-filled splenic flexure could also be demonstrated lying high in the left abdomen close up under the diaphragm, and most striking of all changes in position of the abdominal contents following simple splenectomy, the left kidney was seen to have similarly reverted to normal position as so clearly shown by the postoperative intravenous pyelogram (Fig. 8*b*).

8*a*

8*b*

FIG. 8*a*. Case VI. Intravenous pyelogram showing right kidney in normal position with pelvis of left kidney visualized just to left of 4th lumbar vertebra indicating marked downward and inward displacement of left kidney by huge cystic spleen.

FIG. 8*b*. Case VI. Postoperative intravenous pyelogram showing left kidney reverted to normal position with pelvis opposite 1st lumbar vertebra. Observe also the gas-containing splenic flexure lying close up under left diaphragm.

SUMMARY

1. All of the six cases herein described showed a distinct downward displacement of the splenic flexure to, or below the level of, the hepatic flexure with a variable degree of inward displacement.

2. Three of the six cases showed a pronounced displacement toward the right of the stomach, the other cases showed less pronounced displacement to the right with some compression upon the stomach posteriorly, except in one case which showed no definitely abnormal stomach findings.

3. Two cases showed some associated displacement to the right of the lower end of the esophagus.

4. None of these six cases showed upward displacement of the left diaphragm.

TABLE I

GASTROINTESTINAL ROENTGEN FINDINGS IN SPLENOMEGALY

Case	Physical Examination	Roentgen-Ray (Potter-Bucky) Spleen Measurements	Splenic Flexure	Stomach	Kidney	Esophagus	Left Diaphragm	Gastric Motility	Complicating Features
I. Leucemia	Mass reaching to right of midline and below iliac crest	Length 26.0 cm. Width 11.5 cm.	Downward below level of hepatic flexure	Displaced to right	Normal	No displacement	Normal	Normal	
II. Banti's disease	Questionable spleen or kidney	Length 26.6 cm.	Downward, level of hepatic flexure	Markedly displaced to right with nodular outline	Displaced downward	No displacement	Normal	Small five hour residue	
III. Hodgkin's disease	Hard, movable masses, left upper quadrant	Length 20.0 cm.	Displaced slightly downward	Anterior displacement and compression upper half		No displacement	Normal	Normal	Coexisting retroperitoneal gland masses
IV. Idiopathic splenomegaly (traumatic?)	Not recognized prior to gastrointestinal roentgen examination	Length 20.0 cm. Width 11.5 cm.	Downward, level of hepatic flexure	No appreciable displacement		No displacement	Normal	Normal	
V. Idiopathic splenomegaly	Negative both before and after gastrointestinal roentgen examination	Length 25.0 cm. Width 9.0 cm.	Downward, level of hepatic flexure	Displaced moderately to right		Displaced slightly to right	Normal	Normal	Old pleurisy left lower chest
VI. Splenic cyst	Large fluctuant mass; pancreas? spleen? kidney?	Length 29.5	Downward, slightly below level of hepatic flexure	Entirely to right of midline	Downward and inward	Displaced to the right	Normal	Normal	
Splenic cyst (after removal)			Normal	Normal	Normal	Normal			

5. Of the six cases, in three the left kidney was definitely localized, either by plain films or by pyelography. Two of these showed definite downward displacement of the left kidney but in one case the kidney was not displaced despite marked splenic enlargement.

A rather remarkably complete return to normal position of the displaced stomach, splenic flexure, and left kidney was demonstrated in Case VI after splenectomy by postoperative check-up roentgen studies, although the operation consisted merely of splenectomy. These changes suggest intra-abdominal pressure to be a more important factor than ligamentous support in the maintenance of normal intra-abdominal relationships (Table 1).

CONCLUSIONS

While the gastrointestinal roentgen picture is somewhat variable in the splenomegalies, the displacements of the esophagus, stomach, splenic flexure, and kidney are, nevertheless, rather characteristic. The most constant finding in this series was the displacement of the splenic flexure and, while as already intimated, the picture may be variable, the roentgen findings are usually reliable and clear-cut in the differential diagnosis of splenomegalies from other left upper abdominal tumors.

The writer wishes to express his appreciation to Leo Massopust and Burr Anderson for the illustrations and to Mrs. Evelyn Jensen and Miss Cora Nelson for assistance in preparation of the manuscript.

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ROENTGEN PELVIMETRY*

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FOR many years obstetricians have striven to accurately measure the pelvic inlets of living women. Many methods, not all of them successful, have been described. Such procedures fall roughly into two groups, the mechanical and roentgenologic. Though reasonably accurate, some modern mechanical methods are difficult, and often painful; moreover, if undertaken during labor they are sometimes impossible of fulfillment and always require strict asepsis. To our knowledge, no mechanical method of measuring diameters of the inlet other than the anteroposterior has been devised. External measurements are notoriously deceiving; small birth canals may lie hidden beneath adequate external diameters, and vice versa. Williams states that in two dried pelves with equal true conjugates the external conjugates varied by 5 centimeters. True conjugates in our own patients with external conjugates of 19.5 cm. were found to vary between 8.8 cm. and 12.5 cm.; one patient, with an external conjugate of 23 cm. had a true conjugate of only 10.7 cm. The practice of subtracting 10 cm. from the external conjugate to obtain the true conjugate often results in marked plus or minus variations from the true value.

It would seem, therefore, that roentgenologic methods which are accurate, painless, require no aseptic technique, and can be carried out at any time, even during labor, offer the most in pelvic mensuration.

Various roentgenologic methods have been described. These fall roughly into three main groups—those in which stereoscopic, lateral, or frontal exposures are used. Stereoscopic methods have been described by Archangelsky, Drüner, Chamberlain and Newell with Spalding, Johnson, who has lately adapted the MacKenzie Davidson method to pelvimetry, and others. Although with good films some stereoscopic methods are accurate, certain inherent disadvantages are encountered. Briefly they require twice the exposure and some extra equipment, and unless the patient tilts the pelvis forward as in frontal exposures the promontory is often lost in the shadow of the sacrum. If the pelvis is tilted forward the patient cannot always hold this uncomfortable position during two exposures plus time taken to adjust the apparatus between them. An exclusive advantage of some stereoscopic methods, however, is that the distance between any two visualized points, at the inlet or outlet, can be measured from the same pair of films.

Lateral roentgen pelvimetry has been described, notably by Guthmann, and von Schubert. Theoretically accurate, a disadvantage lies in the frequently so unsatisfactory visualization of the symphysis pubis that this structure cannot be identified. Furthermore only the true conjugate can be measured; the shape of the pelvic inlet is not demonstrated. We agree with others who have shown that, particularly in borderline pelves, the transverse diameter and form of the inlet may be of great importance.

Roentgen pelvimetry by frontal exposure has been described by Martius, Thoms, and others. Advantages are greater simplicity, a larger percentage of satisfactory films, and a clear reproduction of the shape of the inlet. Accurate measurement of the true conjugate is possible in all reliable frontal methods, and with the method of Martius, one can obtain a value in square centimeters for the so-called "plane" of the superior strait, as well as an approximate determination of the transverse diameter of the inlet. As mentioned above, frontal pelvimetric methods do not, as do stereoscopic

* Read before the Obstetrics and Gynecology Section of the California Medical Association, at the Sixtieth Annual Session, San Francisco, April 27–30, 1931.

procedures, permit measurement of the outlet; this can, however, be easily accomplished by the direct mechanical methods in common use. It is our experience, however, that a contracted outlet of sufficient grade to cause any great obstetric difficulty is *in the absence of a contracted inlet* of rare occurrence. Fitzgibbon, on whose service in the neighborhood of 5,000 patients were delivered yearly, states that he has given up routine measurement of pelvic outlets because he considers funnel pelves of no practical importance. We have observed that the shadows of the ischial tuberosities are normally approximately bisected by the projection on to the film of the articular surfaces of the acetabula. A narrowed outlet should therefore be strikingly apparent. One such case was seen in our series. The inlet was also, however, generally contracted to a lesser degree. The full term fetal head readily engaged in the inlet and delivery was easily accomplished with forceps.

Using the method of Martius we have measured the pelves of 125 patients in private practice, consecutive with the exception of two who in times past had had caesarean sections after tests of labor, for contracted pelves. We have analyzed these labors and attempted to correlate them with the roentgenologic findings.

TECHNIQUE

After removing her clothing, the patient dons a gown opening at the back, and a small marker of adhesive plaster is placed in the depression between the spinous processes of the fourth and fifth lumbar vertebrae. She then seats herself in a slouched position over the Potter-Bucky diaphragm, supported by a back rest and her feet braced against a cross bar at the foot of the table. The latter is adjustable to the height of the patient by means of pegs. The tips of the pelvimeter are placed over the adhesive marker and the upper edge of the symphysis pubis, and the patient instructed to arch her back forward. This tilts the pelvis until the anterior and posterior tips are at an equal height as shown by a level fastened to the pelvimeter, thus bringing the true conjugate parallel to the film. The height from the table of the levelled pelvimeter tips is measured and the distance from the table surface down to the film added to this value. The target has been accurately adjusted to 75 cm. above the film, and is now centered by means of a plumb bob over the midpoint of a line between the anterior superior iliac spines. This brings the target approximately over the center of the pelvic inlet. Success depends largely upon scrupulous care in placing the patient and adjusting the apparatus. The patient is cautioned to hold her position, the plumb bob is removed, and the exposure made (Fig. 1).

Fig. 1. Demonstrating the position of the patient on the table.

The result is an enlarged outline of the inlet, taken parallel to the plane in which the true conjugate lies. The latter as represented on the film is measured and from it the actual true conjugate is calculated according to the geometric relationships, as shown in Figure 2.

For this purpose let x represent the true conjugate; a, the measured true conjugate on the film; b, the distance from the target to the film; and c, the distance of the external pelvimeter tips above the film.

Then

$$x:a::b-c:b$$

or

$$x = a\,\frac{(b-c)}{b}$$

Such an equation is solved in a few seconds with a slide rule, and takes only slightly longer by arithmetical processes.

Schaefer and Witte, at Martius' clinic, have proved mathematically that for every focal distance there is an optimum point between the promontory and the symphysis upon which to center in order to minimize the error caused by

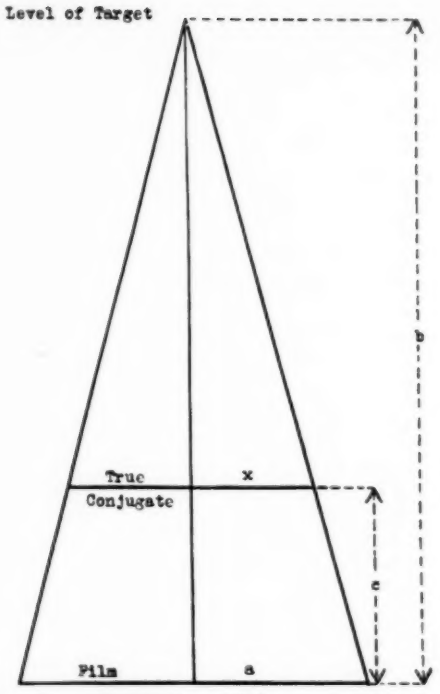

Fig. 2. A representation of the geometric relationships involved in Martius' method.

tipping of the true conjugate forward or backward. They recommend a focal distance of 110 cm. and centering the target over the inner border of the symphysis. If measurements *a*, *b*, and *c* are accurately taken, the maximum error possible with a true conjugate of 10 cm. would be 3.5 mm.

This is a recent refinement of technique of which we have hesitated to take advantage for sake of uniformity in this series.

The transverse diameter of the inlet as represented on the film cannot properly be measured and then corrected as in the case of the true conjugate, because by observing a dried pelvis it is seen that these two diameters do not lie at the same level. The pelvic inlet should not be referred to as "the plane of the superior strait" because the various points on the iliopectineal line bordering the inlet do not lie in the same plane. In studying the dried adult female pelvis, however, we found that the level occupied by the transverse diameter of the inlet closely approaches an average of 2.5 cm. below that of the true conjugate. We found by experimental calculation that for the average transverse diameter, with the usual focal distance of 75 cm., a variation of 0.5 cm. either too high or too low will give an error of usually less than 3 mm., which is obstetrically of no practical significance. We have felt justified, therefore, in calculating approximate transverse diameters of the inlet according to the above equation, first subtracting 2.5 cm. from the value *c*.

Oblique diameters of the inlet cannot be accurately approximated. Their extremities do not lie at the same level, the posterior, at the sacroiliac synchondroses being considerably lower than the anterior, at the pubic spines. These diameters, then, lie at an angle to the true conjugate. After considering experimental calculations with measurements of dried pelves, we are of the opinion that oblique diameters can be estimated with an error of not more than 5 or 6 mm. This approximation may be of advantage in some cases, especially since without the use of roentgen rays no method for measuring this diameter is available. For this calculation we have subtracted 1.5 cm. from the value *c*.

Martius advocated the practice of determining the area of the plane of the inlet from these films. Since the iliopectineal line is irregular, its various points lie at different levels in respect to the film when the exposure is made; consequently various parts of the roentgenographic outline are enlarged to different degrees. Furthermore, as mentioned the inlet is not a plane, it is a *space*. One cannot properly speak, therefore, of an *area* in respect to this space, nor can one accurately measure it from its imperfect image projected on to a plane surface (i.e., the film). From a *practical* standpoint, however, we consider it well worth while to obtain a *value in square centimeters* of the inlet as shown on the film, and then reduce it according to the formula expressing the rate of divergence of light.

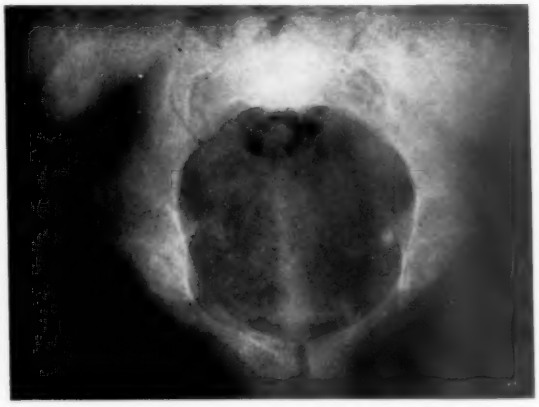

Fig. 3. Normal pelvis.

The area of the inlet on the film is quickly determined with a planimeter, or it can be done by tracing the outline on millimeter-ruled paper over a light box. The number of whole and part square centimeters enclosed can then be totaled. The final value, or "area," can then be calculated according to the equation:

$$A : y :: (b - c)^2 : b^2$$

or

$$A = \frac{y(b - c)^2}{b^2}$$

wherein A represents the desired "area"; y, the area of the inlet on the film; b, the distance from the target to the film and c, the height of the pelvimeter tips above the film.

DISCUSSION

The average values for the various measurements in our cases are as follows: areas 113.8 sq. cm., true conjugates 11.4 cm., transverse diameters 13.2 cm. If the cases requiring caesarean section for contracted pelvis are deducted, the averages are: areas, 114.1 sq. cm., true conjugates 11.4 cm., and transverse diameters 13.3 cm.

From anatomical studies of the adult white woman the normal length of the true conjugate is given in most textbooks at about 11.5 cm., and that of the transverse diameter of the inlet at approximately 13.5 cm. Our roentgen averages correspond closely to these figures. From roentgenologic data, we consider the area to be normal between 110 and 120 sq. cm.

Comparing the labors in this series with the roentgen measurements, we found a definite relationship to the necessity for abdominal delivery. Ten caesarean sections for contracted pelvis were performed; four of these had had previous sections. Test of labor to demonstrate engagement or nonengagement of the head was given whenever advisable, but the following illustrates the necessity of caution in patients who had previously had a caesarean section. Low caesarean section was performed after no engagement of the head during three and one-half hours of labor, on a patient who had had a previous low caesarean. A weak spot in the old uterine scar was found which ruptured with only slight pressure of a finger. Another patient who had had a previous classical section was found on elective low section to have a small rupture of the old scar without even going into labor at all. Seven patients who had had caesarean section were allowed a test of labor.

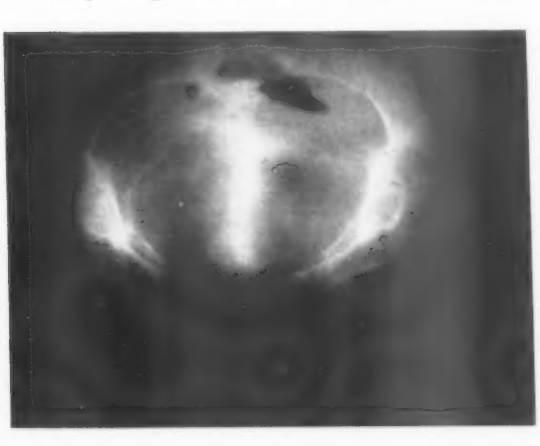

Fig. 4. Flat pelvis. C.V., 8.8 cm.; trans., 14.6 cm.; obstetrical index, 128; area, 110 sq. cm.

Table I

CAESAREAN SECTIONS IN RELATION TO TRUE CONJUGATES

True Conjugate	No. of Cases	No. of Caesareans	Test of Labor	Per Cent
8.5– 9.0	1	1	0	100
9.0– 9.5	5	3	3	60.0
9.5–10.0	9	3	2	33.3
10.0–10.5	11	2	1	18.2
10.5–11.0	18	0	0	0
11.0–11.5	23	1	1	4.3
11.5–12.0	26	0	0	0
12.0–12.5	16	0	0	0
12.5–13.0	12	0	0	0
13.0–13.5	4	0	0	0

Table I classifies the cases requiring caesarean section in relation to the true conjugate and Table II in relation to the transverse diameters of the inlet. The graph shown in Figure 5 shows them in relation to the area and the obstetric index (described below). These curves are reasonably smooth with the exception created by one patient with an area of 110 sq. cm., a true conjugate of 11.4 cm., and a trans-

TABLE II
CAESAREAN SECTIONS IN RELATION TO TRANSVERSE DIAMETERS

Transverse Diameter	No. of Cases	No. of Caesareans	Test of Labor	Per cent
11.0–11.5	2	0	0	0
11.5–12.0	6	2	2	33.3
12.0–12.5	14	3	2	21.4
12.5–13.0	30	2	2	6.7
13.0–13.5	28	1	0	3.6
13.5–14.0	26	2	1	7.7
14.0–14.5	14	0	0	0
14.5–15.0	3	0	0	0
Over 15.0	2	0	0	0

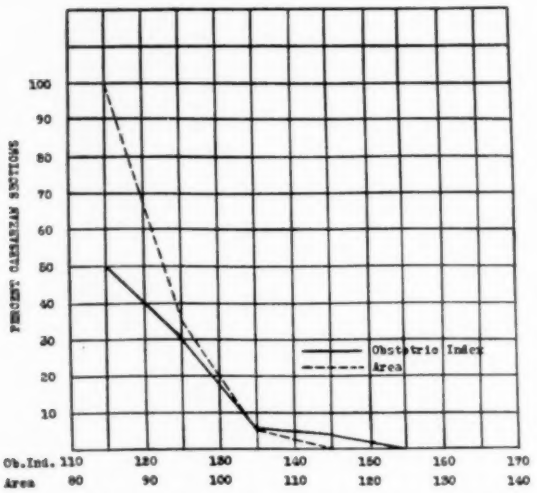

FIG. 5. Graph illustrating relationship of caesarean sections to area and obstetric index in a series of 125 cases.

verse diameter of 12.8 cm. With measurements apparently ample no difficulty was anticipated. Test of labor with good pains failed to engage the fetal head, and she was finally delivered of a normal baby weighing 8 pounds 5 ounces, by low caesarean section. Just why the head failed to engage we do not know, but it was probably a case of unrecognized brow presentation.

The cases were also studied to determine possible relationship between the size of the pelvis, or any single diameter thereof, and the incidence of mid-forceps applications, also its relationship to the length of labor. As we expected, no demonstrable relationships existed, due, no doubt, to various extraneous factors after engagement of the head, such as the strength of uterine contractions, the rigidity of the cervix and other maternal soft parts, the position and size of the fetal head, and other considerations.

No application of forceps above the brim was attempted; there were no versions; 3 were breech presentations and deliveries. There was no difficulty referable to contraction of the outlet.

Martius, from his experience, considers an area of 80 sq. cm. in a generally contracted pelvis the smallest through which a full term fetal head can pass, and then only with great difficulty. In flat pelves, particularly those with a prominent promontory, the area may be much greater than that, with a true conjugate too short to allow passage of the full-term head. In such cases, of course, knowledge of this measurement is all that is necessary to decide that delivery by the natural passage is impossible. Martius places the unsurmountable true conjugate at 7.5 cm. and below, including allowance for that important and often neglected factor, molding of the fetal head. In flat pelves of moderate grade without undue prominence of the sacral promontory, the area and the transverse diameters may be deciding factors. There may be enough lateral space to allow the smaller bitemporal diameter of the head to pass the true conjugate, rather than the larger biparietal.

The majority of abnormal pelves encountered in this series were of the generally contracted variety. True flat pelves of more than moderate degree were not seen, due undoubtedly to the fact that advanced rickets is not as often encountered in patients in private as in clinic practice, nor is it common in this locality.

Since available lateral space is often of such importance in contracted pelves with no diameter too short to preclude natural delivery in itself, we have, in addition to the measurements advised by Martius, taken products of true conjugates and

transverse diameters, and plotted them in gradations of 10 against the percentage of caesarean sections necessary in each category. To illustrate: The true conjugate of a given pelvis measures 10.5 cm. and the transverse diameter of the inlet 13 cm.; both are somewhat below the average. Multiplying these figures we obtain a product of 136.5. The graph, illustrated in Figure 5, suggests that difficulties in engagement may begin when this product approaches 135 to 140. Of course further experience will be necessary to settle this point. Although this is a very small series, we believe that the curve represents approximately what one may expect to be the outcome in cases of contracted pelvis. We consider a product of between 150 and 160 as the average normal. The largest in this series was 210, the smallest, 111.

Because of the fact that the outline of the inlet is, as explained above, slightly distorted, and a true "area" of the inlet cannot be obtained, we believe that such use of the most important and reasonably accurate measurements will result in an arbitrary figure which best expresses the conditions at hand. This seems all the more true when we consider how "standard" other parts of the iliopectineal line are. Except in cases of gross deformity or injury, recognizable at a glance, the superior rami of the pubes and the regions of the sacroiliac synchondroses have much the same curves in all cases. While the "area" of Martius includes some useless space, the product of the true conjugate and transverse diameter, which we have called the *obstetric index*, is arrived at by the use of obstetrically significant measurements only.

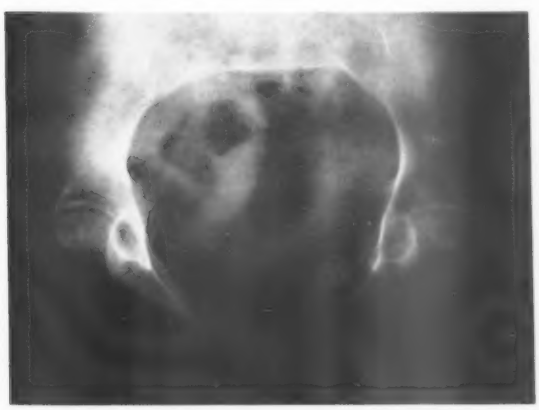

Fig. 6. Fracture of pubis encroaching upon birth canal.

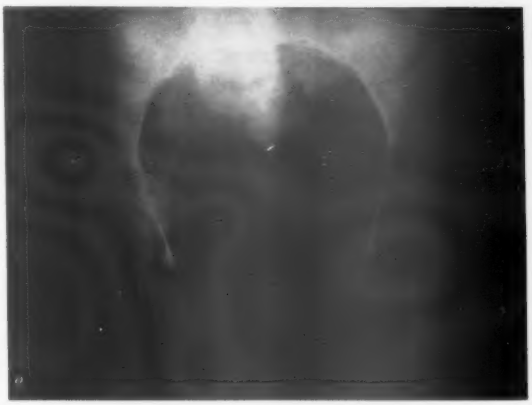

Fig. 7. Spondylolisthesis.

We intend to calculate both the "area" and the obstetric index for some time in the hope of deciding definitely if consideration of the less exact "area" can safely be dispensed with.

The following case not included in this series illustrates how large a baby will pass through a justo major pelvis of only *moderate* degree. This patient gave birth *spontaneously* to a baby weighing 14 pounds 10 ounces whose measurements were B.T. 9.5 cm., B.P. 10.75 cm., S.O.B. 11.5 cm., length 67 cm. The maternal pelvis measured: C.V. 12.6 cm., transverse 15 cm., area 135 sq. cm., obstetric index 189. The patient gave a history, only partially confirmed, of spontaneous deliveries of babies weighing up to 20 pounds.

We believe Martius' method of roentgen pelvimetry gives reliable information as to whether a normal head in normal position will pass through a given pelvis; and if the progress of labor with an adequate pelvis is not normal, other factors such as anomalies of flexion or rotation should be sought and corrected according to the teachings of the art of obstetrics.

SUMMARY

1. External pelvimetry is not reliable as a guide to the size of the pelvic inlet.

2. We consider some roentgen pelvimetric procedures to be far superior to any internal mechanical method.

3. The method of Martius, which we consider most satisfactory, is described.

4. The labors of 125 patients are analyzed and compared with the roentgenologic findings.

5. The possible prognostic value of the "obstetric index," a product of the true conjugate and transverse diameter of the inlet, is suggested.

6. We believe that a pelvimetric method such as described best demonstrates abnormalities and injuries of obstetric significance.

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Vol. XXIX, No. 4

ON THE NATURE OF THE TUBO-UTERINE SPHINCTER
AN EXPERIMENTAL STUDY

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DURING recent years the science of gynecology has enriched itself with two new methods of investigation; the first is the insufflation of the Fallopian tubes and the second is salpingography. Both the methods, especially the latter, apart from their being diagnostically important, have proved to be useful in throwing a new light on many anatomo-physiological questions partly debatable, partly unsolved, and definitely not established, making them more clear.

To these the question of the nature of the tubo-uterine sphincter should be referred.

According to literary data, a long while ago the Fallopian tubes were supposed to have two sphincters: one in the region of the ostium uterinum tubae, and another in the region of the ostium abdominale tubae. To distinguish them from one another we call the former sphincter tubo-uterinus, and the latter sphincter tubo-abdominalis. The present study deals exclusively with the sphincter tubo-uterinus.

The hypothesis of the existence of the above-mentioned sphincter was first stated as early as 1858 by the French professor, Aran,[1] who in his clinical lectures wrote as follows: "Les orifices (uterins) des trompes sont certainement pourvus d'un sphincter, et la contractilité de ce sphincter doit s'apposer pendant la vie a la penetration des liquides dans la trompe et par elle dans la peritoine." Aran gave, however, no objective data to confirm his hypothesis.

Somewhat later, namely, in 1862, the German scientist, Hennig,[15] in describing the muscular layer of the Fallopian tubes said: "At this point, that is, the uterine aperture (ostium uterinum) of the tubes, the outmost layer of the circular fibers is interlaced with the longitudinal fibers." In this way, after Hennig, the presence of the tubal sphincter suggested by Aran, was sufficiently proved.

Here the obvious tendency of Hennig is felt to give some anatomical basis for the interpretation of the tubo-uterine sphincter, i.e., to prove and explain its existence by means of a definite anatomical structure of the muscular layer of the tubes in the region of the ostium uterinum tubae.

These are practically all of the data that we have in the older literature concerning the tubo-uterine sphincter.

Among the subsequent authors there are only a few who restrict themselves with the mere mention of the tubo-uterine sphincter; some of them (Bandl,[4] Lazarevitch[24]) consider the existence of the sphincter to be a well-established fact; others think that it has not been proved (Oertel[29]). The great majority of writers, however, are likely to ignore the tubo-uterine sphincter and do not mention it at all.

Such was the position in which the question remained up to the introduction of the uterotubal insufflation and salpingography. With the appearance of these two methods the time has come when the tubo-uterine sphincter is, as it were, rediscovered once again. If we refer to the bibliography of the subject, we shall see that the way to this rediscovery has been gradually paved.

The observations and investigations of various authors who had applied gas insufflation of tubes and salpingography within four or five years (1922–1926) have consistently suggested that generally in the Fallopian tubes, and particularly in their interstitial section, there was some hindrance which prevented the gases and fluids from passing from the uterine cavity

into the tubal canals. There was no agreement, it is true, in the interpretation of this hindrance. Some explained it as a result of the narrow lumina of the tubes (Sellheim[42]); others explained it by the swelling of the mucous membrane of the interstitial portion of the tubes (Guthmann[14]); others, by the spasm of tubes (Rubin,[33,34] Kennedy,[21] Peterson[30]) or by the spasm of the sphincter-like circular muscle in the interstitial portion of the tubes (Meaker[25]); another group, by the sinuous (winding) direction and of the interstitial portion of the tubes (Geist[11]); others, by the valve-like closing of the interstitial portion of the tubes (Frommolt[10]), and still others, by the presence in the tubes of some delicate mechanism—a sort of a barrier, meaning by this the tubal contractions (v. Mikulicz-Radecki, Lueg and Nahmmacher[27]).

Nevertheless, despite the diversity in the interpretation, all of these observations had emphasized one and the same fact—that of the existence in the tubes of some impediment, of some barrier; by drawing the attention of the investigators to this barrier they have, so to speak, put landmarks, cleared and paved the way to the rediscovery of the tubo-uterine sphincter.

It was Reinberg and Arnstam,[31] Russian scientists, who in 1926, with objective and demonstrative data in their hands, first came forward as advocates of the existence of the tubo-uterine sphincter.

Applying hysterosalpingography to the living, Reinberg and Arnstam, in a series of roentgenograms, succeeded in fixing the tubo-uterine sphincter most clearly and distinctly. Their discovery, which was never published by any one before, was reported by them before the Fourth All-Union Conference of Roentgenologists and Radiologists in Leningrad, on May 22, 1926.*

Demonstrated by Reinberg and Arnstam, the tubo-uterine sphincter has since been, within a short period of time, confirmed by a series of subsequent writers (Bakke,[2,3] Romcke,[32] Heuser,[17] Hermstein,[16] Saidl,[38] Odischaria and Zakrjevsky,[28] v. Mikulicz-Radecki and Freund,[26] Ginsburg and Strokoff,[12] Janaky,[18] Rubin,[35,36] Gosset, Ledoux-Lebard and Béclère,[13] Schultze,[41] Jarcho,[19] Cotte,[6] Witwer, Cushman and Leucutia[43]).

Notwithstanding the numerous observations which have fully confirmed the existence of a tubo-uterine sphincter there have been, and are now, skeptics among gynecologists who doubt or even deny the existence of a tubo-uterine sphincter.

Thus Joachimovits[20] says that, at least beyond the period of menstruation, there is no mechanism for the closing of tubes.

Denying the existence of a genuine sphincter, Elektorowicz and Zawodzinsky[8] admit only the existence of a pseudo-sphincter.

Some writers consider the constrictions, formed in the place where the tubes begin, not to be a sphincter but a result of peristaltic contractions of either uterus (Dyroff[7]) or tube (Fraenkel,[9] Kok[22]).

The cited opinions show that even the very fact of the existence of a tubo-uterine sphincter has not been unanimously acknowledged among gynecologists, but is discussed and even denied by some authors who, it is true, are in the minority.

Passing, further, to the question as to what the nature of the tubo-uterine sphincter is, we should recognize that, up to the present time, it is far from being quite clear and remains, we may add, completely unsolved.

With respect to the nature of the tubo-uterine sphincter, two conjectures are possible: the tubo-uterine sphincter is either a functional apparatus or an anatomical structure.

Below we give the references to the literature on the subject.

The majority of gynecologists ignore the question of the nature of the tubo-uterine sphincter, and only a few of them make any attempt at its solution.

* Apart from Reinberg and Arnstam, and independently of them, Schneider and Eisler[40], German scientists, determined, in the same way, the existence of the tubo-uterine sphincter, but their report appeared later.

Thus, Reinberg and Arnstam[31] believe that the tubo-uterine sphincter is a result of a tonic contraction of circular muscular bundles, and try to prove this statement by their rare (and scanty) observations upon pregnant women, whose uterus is atonic. In 3 of their cases, where lipiodol penetrated tubes, they observed the broad communication between the uterine cavity and lumen of the tubes, but they did not see any narrowing of the lumen at the ends of the intramural portion of the tubes. Hence, Reinberg and Arnstam deduced that the tubo-uterine sphincter is a functional apparatus.

Similarly, Hermstein[16] considers the sphincter to be a functional closing of the tubes owing to the spastic contraction of muscles and admits that not only circular but also longitudinal muscular fibers take some part in this contractile effect.

Schneider and Eisler[39,40] declare themselves for the functional character of the sphincter and to prove this they refer, on the one hand, to the analogy with the pylorus of stomach, where constrictions also exist and where they are accounted for by a special innervation, and not by the anatomical sphincter, and, on the other hand, they point out that the existence of the anatomically strong muscles have not been proved in the region of the sphincter.

In addition, we were fortunate enough to find in the literature on the subject some indications as to the anatomical nature of tubo-uterine sphincter.

In a series of sections Romcke[32] discovered a restricted bundle of the circularly arranged muscular fibers, which in its position corresponded to the constriction that is usually obtained on the roentgenograms; such a discovery could be taken as the evidence of the anatomical substratum of the sphincter, but studying simultaneously the results of the injection of lipiodol into the isolated uteri with their subsequent roentgenography, Romcke failed to demonstrate the presence of constrictions on the roentgenograms which was in itself the confirmation of a quite different conjecture, notably, that here we have to deal not with the anatomical structure, but the contraction of the annular muscles—otherwise that the tubo-uterine sphincter is a functional apparatus.

This reference to the literature shows that the few writers who have studied the question of the nature of the tubo-uterine sphincter almost unanimously state that its character is functional. The reasons which they adduced to prove their opinions are, however, not entirely convincing as well as not quite capable of demonstration.

Thus, the question as to the nature of the tubo-uterine sphincter has remained open up to the present time.

In approaching the solution of this interesting and rather obscure question we were guided by the following reflections: If the tubo-uterine sphincter is a functional apparatus, i.e., if it owes its existence solely to the contractions of muscles, then it is a provisional structure occurring only at the moment of the contraction of the tube or the uterus; the sphincter may be formed upon the contracted tube or uterus, but it can never appear on the relaxed organs. Hence the deduction results that we can and should never obtain the sphincter on the dead organs deprived of the capacity for any contraction whatever.

Conversely, if the tubo-uterine sphincter is an anatomical structure having fundamentally a definite anatomical formation, it should be a more or less constant formation and, being independent of muscular contractions, might be obtained on the organs that have relaxed muscles; we should be able, therefore, to obtain this kind of an anatomical sphincter in certain cases, at least in those where the sphincter is distinctly pronounced, even upon the dead organs that are deprived of any functional capacity, but preserve its anatomical structure.

With this in mind we decided to carry out hysterosalpingography systematically upon the organs removed at operation on account of some disease and, in addition, a more or less long time after their removal.

Before we discuss the results obtained, let us take up the technique of our research.

When doing a hysterosalpingography upon the isolated organs, we could not, naturally, expect that the contrast fluid introduced into uterine cavity would be forced into the tubes by means of the contractions of the uterus, but we should rely here only upon the strength of the pressure applied. It could therefore be foreseen that sometimes the pressure would have to be raised up to a considerable height. If it be so, one must be particularly careful about an accurate, hermetical closing of the cervical canal.

With the isolated organs before us, i.e., organs which were seemingly deprived of their capacity to contract, the organs relaxed and flabby, whose cervix was, in addition, not infrequently deformed and semi-destroyed by a cancerous process, it was impossible to expect to obtain hermetical sealing in all of the cases with the aid of the common uterine cannula, which has been usually applied, and closes only the os externum uteri. We have had, therefore, to construct a special cannula which allowed us to close not only the os externum, but the cervical canal at any point of its extension.

It could be attained with the aid of an insufflated "rubber bullet" attached to the cannula. By means of such a cannula, in all cases regardless of the condition of the os externum, a reliable hermetical sealing has been attained, the reflux was precluded and we were able to raise the pressure to the desired height.

As a constrast fluid we used first iodipin (Merck) but this was found to be too expensive as well as not so convenient because not infrequently, owing probably to the density of the preparation, we failed to force the iodipin into the tubes; as a result we soon began to use the dilute aqueous solution of sodium bromide (natrii bromati), but in this case, also, the solution was found to have another disadvantage, although it penetrated the tubes more easily, namely: when the tubes were open and the solution entered them a large amount of it soon poured out, obscuring the picture of the subsequent roentgenogram; this was unsatisfactory. We had, therefore, to look for still another contrast medium and, after considerable search, we chose the 30 per cent emulsion of bismuth subnitricum; it penetrated the tubes more easily than iodipin, and did not leave the tubes so quickly as the aqueous solution natrii bromati. This enabled us to obtain the roentgenogram earlier. We preferably used the 30 p.c. emulsion for filling isolated uteri and tubes.

The filling of the removed organs by the contrast fluid was achieved with the aid of pressure; this was measured by means of a spring manometer attached to the uterine cannula through the so-called "basal tube" proposed (invented) by me.[5]

The organs removed at the time of the operation (uterus with one or both tubes) were placed in a jar of water at room temperature and kept there until the hysterosalpingography had been done. No measures were taken to support life in the removed organs and, owing to their being kept in water, they were quickly subjected to processes of decay.

The organs were taken out of the water immediately before hysterosalpingography, then dried by means of cotton pledgets and placed at the beginning, on a glass plate, and afterwards simply on a sheet of paper, being arranged in the horizontal plane.

All of the roentgenograms were taken in the Roentgen Department of the Institute of Physiotherapy, Tomsk, Siberia, by means of a Heliopan apparatus (Reiniger-Gobert-Schall) and Coolidge Media Hochleistung Müller tube; hardness 8 Wehnelt; the distance of the tube from the surface of the preparation 60 cm., the duration of the exposure one to one and a half seconds. By filling the isolated organs with the contrast fluid and immediately taking roentgenograms we succeeded in fixing the tubo-uterine sphincter on a series of roentgenograms. Presenting here some of them, we give, as briefly as possible, the data

which may be of service in a correct understanding and interpretation with respect to the tubo-uterine sphincter. We shall not, however, touch other details which are present on the roentgenograms and are perhaps of some interest but bear no direct relation to the tubo-uterine sphincter.

Case I. M. M., aged thirty, admitted to the Gynecological Clinic on November 14, 1927. Diagnosis: cancer of cervix uteri (Clinical Register N 264).

On November 21 the Wertheim operation was performed under general mixed chloroform-ether anesthesia (as in all of the other cases); the uterus with both the tubes and ovaries was removed from the abdominal cavity at 11:30 a.m. and immediately placed in the jar of water.

On the same day at 7:30 p.m., i.e., just eight hours after the removal of the organs, 5 c.c. of slightly warmed 40 per cent iodipin (Merck) was introduced into the uterine cavity, pressure 180 mm., and a roentgenogram was taken (Fig. 1).

We see on this roentgenogram that the upper corners of the uterine cavity have each at their tops on both sides one sharply outlined annular constriction; it is this constriction which is the tubo-uterine sphincter; on either side laterally of the sphincter a dilatation is seen having on the right the shape of a cupola; narrowing abruptly, this latter, suddenly in several spirals, passes into the filiform lumen of the tube; on the left, the dilatation has a shape of a cone which is turned with its base to the uterine cavity, and with its gradually narrowing top passes into the lumen of the tube.

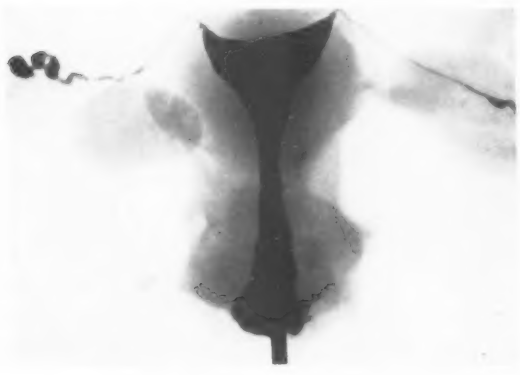

Fig. 1

Fig. 2

Case II. M. M., aged fifty; admitted to the clinic on April 13, 1928, for cancer of cervix uteri (Clinical Register N 127).

On April 19 a Wertheim operation was done. The uterus and both the tubes and ovaries were taken out at 11:40 a.m., and placed in a jar of water.

On April 20, at 12:40 p.m., i.e., twenty-five hours after the isolation of the organs, 6 c.c. of 30 per cent emulsion of bismuth was introduced into the uterine cavity, pressure 150 mm. and a roentgenogram was taken (Fig. 2).

The roentgenogram shows sufficiently clearly that on the borderline between the cavity of the right horn of the uterus and the interstitial section of the right tube there is a distinct annular constriction, which is the tubo-uterine sphincter; then the pear-shaped dilatation follows which further passes into the filiform lumen of the interstitial part of the tube; on the left, at the top of the uterine horn there is only slight suggestion of the constriction which is more distinctly pronounced on the side of the edge of the uterus.

After hysterosalpingography, the uterus with the ovaries was put in a 10 per cent solution of chloral hydrate, prepared with distilled water. After the organs had remained in this solution for twenty-four hours, and forty-nine hours after their isolation, the uterus was refilled with 30 per cent emulsion of bismuth at pressure 180 mm., and another roentgenogram was taken (Fig. 3).

This shows, on the whole, the same picture as the previous one, differing from the latter in the following: first, in Figure 3 the constriction representing the right tubo-uterine sphincter is less deep, so that the sphincter seems to be, as it were, somewhat dilated; secondly, on

Fig. 3

Fig. 5

the left, the tubo-uterine sphincter, as well as the dilatation which is situated laterally, is more distinctly seen, and thirdly, in the uterine wall in the region of the right horn a network is seen consisting of thin, branching anastomosing canals which were formed by the contrast fluid that penetrated them.

Case III. P. A., aged thirty-five; admitted to the Clinic on April 24, 1928, for an operation for cancer of cervix uteri (Clinical Register 2946 N 138).

On April 28 the operation was done; the uterus with the left tube and ovary, as well as the right tube, was removed from the abdominal cavity at 12 o'clock (noon); the right overy was left in situ.

On May 2, at 1 p.m., i.e., more than four days (97 hours) later, the removed organs were filled with the 30 per cent emulsion of bismuth; first 4 c.c. of emulsion was introduced and at a pressure of 80 mm. a roentgenogram (Fig. 4) was taken; then 3 c.c. more of the emulsion was added (7 c.c. in all) and at a pressure of 300 mm. another roentgenogram (Fig. 5) was taken.

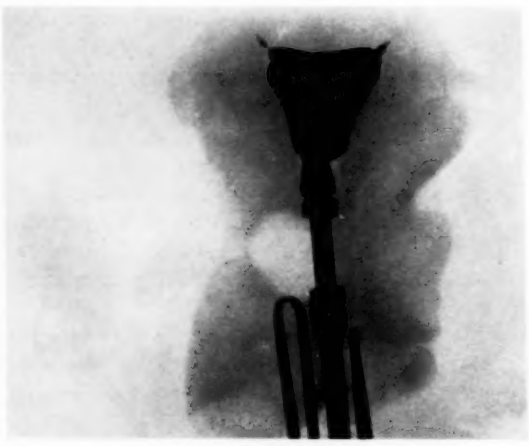

Fig. 4

On both the roentgenograms we see distinctly pronounced tubo-uterine sphincters; on the left, the sphincter is more sharply pronounced and almost fully separates the uterine cavity from the lumen of the tubal canal; in Figure 4 (pressure 80 mm.) only the tubo-uterine sphincter is seen as well as the subsequent dilatations, while in Figure 5 (pressure 300 mm.) the lumina of the tubal canals are also visible, and on the left, where the sphincter is more sharply pronounced, the tube has been outlined at the shorter distance and the amount of the contrast fluid which has penetrated its lumen is less than on the right; at the lower side of the roentgenogram, just above the left crow-bill an oval shadow is seen of the insufflated rubber bullet at the uterine cannula.

Case IV. B. R., aged thirty-one, admitted to the clinic on May 3, 1928, for operation for fibroma of the uterus (Clinical Register N 146).

On May 5 at 1 p.m., a supravaginal amputation of the uterus was done and both the tubes were removed; the organs just after removal were placed in a 10 per cent aqueous solution of chloral hydrate.

On May 9 at 12:30 p.m., i.e., four days later (more precisely after 95 hours 30 minutes) 9 c.c. of a 30 per cent emulsion of bismuth was introduced into the uterine cavity, and at a pressure of 260 mm. a roentgenogram was taken (Fig. 6).

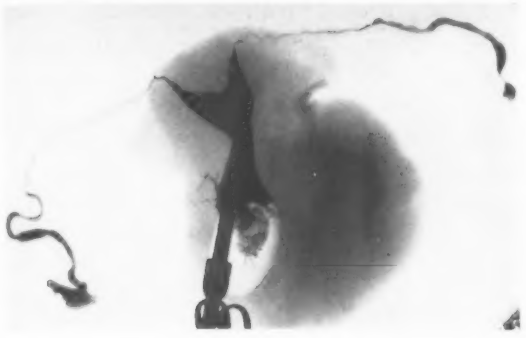

Fig. 6

One can distinctly see on this roentgenogram that the conically extended upper corners of the uterine cavity on both sides are separated from the tubal lumen by construction, i.e., the tubo-uterine sphincters; the constriction is more pronounced on the right and, being likely to depend upon the amount of contrast medium entering the right tube, seems to be less as compared with the left tube; below the roentgenogram the shadow of the insufflated rubber bullet is seen.

Case v. B. Z., aged fifty-two, admitted to the clinic on September 19, 1928, for operation for cancer of the cervix uteri (Clinical Register N 175).

On September 22 the Wertheim operation was performed and the uterus with its adnexa was removed at 11:30 a.m.

On September 26 at 11:30 a.m., i.e. after ninety-six hours, or four days, 6 c.c. of 40 per cent iodipin was introduced into the uterine cavity and at a pressure of 350 mm. a roentgenogram was taken (Fig. 7). Then, two days later, September 28 at 9:30 a.m., i.e., 142 hours after the removal of the organs from the abdominal cavity, or almost six days after, hysterosalpingography was repeated on the same organs; 8 c.c. of iodipin was introduced, and at a pressure of 350 mm. another roentgenogram was taken (Fig. 8). When the hysterosalpingography was over, the organs were placed in a 10 per cent aqueous solution of chloral hydrate and six days later, that is, on October 4, at 9:30 a.m., i.e. almost twelve days later (286 hours after the removal of the organs from the abdominal cavity), hysterosalpingography was repeated once again; this time 9 c.c. of bismuth emulsion was introduced, and at a pressure of 300 mm. the roentgenogram shown in Figure 9 was taken.

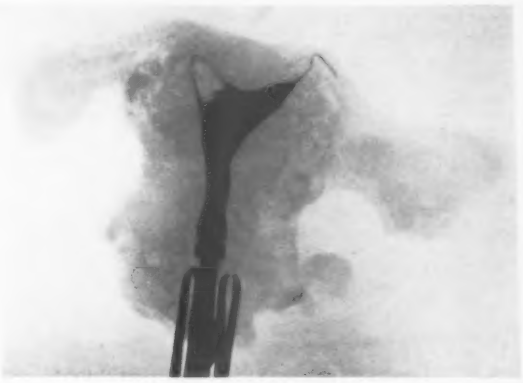

Fig. 7

On examining the roentgenograms presented, we see that on the left neither tubo-uterine sphincter nor lumen of the tube is seen in Figure 7, which may be explained by the filling up with air of the left horn of the uterus, whereas on the right the tubo-uterine sphincter is rather distinctly outlined in the form of an almost annular constriction, which is followed by a small conical dilatation passing into the filiform lumen of the right tube; this latter is filled with the contrast fluid and is visible only in its interstitial and partly isthmic section.

In Figure 8 the right tubo-uterine sphincter, as well as the right tube, appears as in the previous roentgenogram. Besides, the left tubo-uterine sphincter is distinctly outlined and the left tube is filled up with contrast medium.

In Figure 9 the right tubo-uterine sphincter is not plainly seen, but the left one stands out more distinctly.

We have, moreover, a series of roentgenograms with the tubo-uterine sphincter on the isolated organs but some technical considerations prevent us from publishing them. The

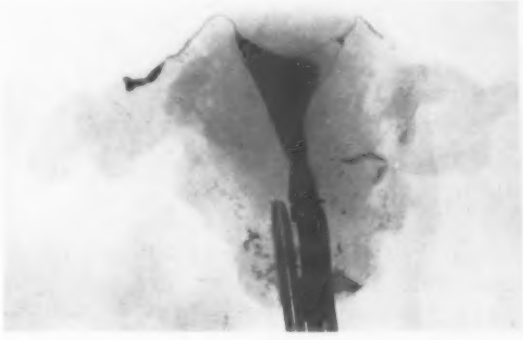

Fig. 8

roentgenograms which are shown here are sufficient, we believe, to prove the statement upon which the present report is based.

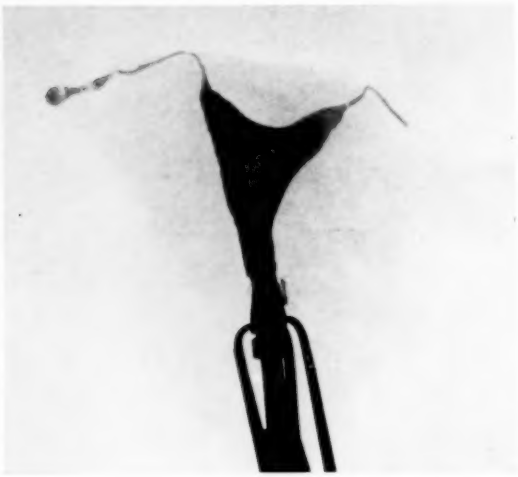

Fig. 9

Summing up our findings we can state the following considerations:

We placed the female reproductive organs removed at operation (the uterus and the tubes) in a jar of water, pursuing in this only one aim, viz., to prevent these organs from drying and thus to secure the possibility of easier and more convenient filling with contrast fluid; we took no measures to support life in the isolated organs; on the contrary, in particular cases some measures were taken to destroy any functional capacity of the organs (placing them in the solution of chloral hydrate).

After filling the organs with the contrast fluid they were roentgenographed at various intervals of time after their removal from the abdominal cavity: eight hours (Fig. 1), twenty-five hours (Fig. 2), forty-nine hours (Fig. 3), ninety-five hours thirty minutes (Fig. 6), ninety-six hours (Fig. 7), ninety-seven hours (Figs. 4 and 5), one hundred and forty-two hours (Fig. 8), and two hundred and eighty-six hours (Fig. 9).

In all of them a distinct shadow of the tubo-uterine sphincter was obtained.

We are now asking if the roentgenograms obtained are able to throw any light upon the nature of the tubo-uterine sphincter. Can they show whether the tubo-uterine sphincter is a functional apparatus or an anatomical structure?

To answer this question it should be first established whether the organs we had experimented on are functionally active, i.e., are capable of some contractions, or whether they are functionally inactive and are unable to contract.

In the literature available we failed to find out the direct indications as to how long the human uterus and tubes, after their removal from the body, can retain their capacity to contract unless measures are taken to maintain their activity.

Koordinofsky,[23] in experimenting upon the isolated uteri of rabbits through which Locke's solution had been passed, observed that "in one case the uterus lived for forty-nine hours forty minutes." But this uterus was one, to keep the life in which a series of special measures had been taken, and in addition it was a rabbit's uterus. Although we believe it impossible to transfer in their entirety the experimental results obtained in the rabbits to women, nevertheless Koordinofsky's experiments enable us to suppose that the uteri and tubes of women which were subjected to our investigations and in which no measures were taken to keep them alive, could hardly retain their functional capacity for even two days. It is, however, only a mere conjecture.

To approach the subject more objectively Dr. A. D. Timofeyefsky (now Professor of Medical College, Omsk, Siberia) and myself have conducted, in the pharmacological laboratory of Prof. N. W. Versheenin, some experiments to ascertain how long the muscular tissue of the isolated human uteri and tubes kept without any preventive measures can respond to various kinds of irritation. With this in mind the uteri and tubes isolated at the time of the operation were placed in a jar of water and kept there at the room temperature, before the experiment, during a more or less long period of time. Just before the experiment the interstitial section of the

tube, together with the muscular wall of uterus, was cut out so that pieces 2–3 cm. in length and about 0.75–1 cm. across were obtained. The pieces were stimulated by means of the inductive current, adrenalin, pilocarpine, ephedrine, barium chloride, and secale cornutum. We have obtained the following results: eight hours after the uterus, together with tubes, was removed from the body, one could in only one case after stimulating the isolated pieces discern a slight elevation of the tonus, as well as hardly noticeable waves of contraction; twenty hours and more later in no case could either the elevation of the tonus or any waves of contraction be noticed.

These experiments showed that the cut out pieces of the muscular wall of the uterus together with the interstitial section of tubes at least twenty hours after their removal from the body lost their functional capacity and did not react by contraction even to intense stimulation.

If twenty hours after their removal from the body the muscular tissue of the uterus and the interstitial section of the tubes, even despite the use of the intensive irritants proved to be devoid of their contractile capacity, it was all the more so with uteri and tubes four, six, and twelve days, after their removal.

These organs which in the meantime have undergone processes of disintegration and decay should be considered functionally dead and unable to contract. Nevertheless, on losing their contractile capacity these dead organs, until they disintegrate, should more or less retain their appropriate anatomical structure. The formations obtained on these organs should therefore not be referred to their contractile function, but to their anatomical structure. It was on these dead organs where by means of hysterosalpingography we obtained the tubo-uterine sphincter.

Now the answer to the question that was put before, concerning the nature of the tubo-uterine sphincter is plain, clear, and self-explanatory.

Since the tubo-uterine sphincter, which we have shown on our roentgenograms, was obtained on the dead organs that were unable to contract and were functionally inactive, we must state that the sphincter is not a functional apparatus but an anatomical structure.

Thus, as a result of our studies the Aran-Reinberg-Arnstam tubo-uterine sphincter must be considered as an anatomical structure.

In concluding we can draw the following deductions: 1. The tubo-uterine sphincter does unquestionably exist. 2. In its nature the tubo-uterine sphincter is an anatomical structure, and not a functional apparatus.

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MULTIPLE MYELOMA

AN EVALUATION OF ITS ROENTGEN SIGNS*

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IN THE diagnosis of multiple myeloma no other single diagnostic procedure offers more readily available or more reliable criteria than a well-planned roentgen examination of the patient. The microscopic section, which would naturally supersede a roentgen study in point of absolute accuracy, is often not feasible in this condition. The clinical findings are not consistently subject to interpretation without the disclosures of roentgen study. In instances where the diagnosis of multiple myeloma is unduly delayed, incomplete roentgen examination is at times acknowledged.[11] The University Hospital records of 1910 reveal one case of multiple myeloma not discovered until autopsy; on this occasion, roentgen examination had been omitted, or, at least, no note of such investigation can be found. On the other hand, in another instance when the roentgenogram was accorded the status of final authority in diagnosis, the changes, due probably to syphilis, were misinterpreted as multiple myeloma. However, correct roentgenologic interpretation does offer the most satisfactory method available for diagnosis.

In the literal sense, the term "multiple myeloma" should refer solely to tumors of a multiple character, not limited in type, but necessarily originating in the bone marrow. As a matter of fact, the term "multiple myeloma" is used to denote malignant plasma-cell tumors, whether single or multiple, or found exclusively in parts other than the bone marrow. Lymph gland or bone, if involved by a plasmocytoma, bears the same designation.[19] Still, the classical type of multiple myeloma is a multiple, simultaneous growth of nests of plasma cells in the bone marrow alone—a true plasma-cell myelomatosis.

Multiple myeloma is an infrequent but far from rare disease. It has not been extensively discussed in most textbooks, but the periodical literature contains many references. Through a period of almost sixty years, from the first description in 1848 until 1905, Charlton[10] found reports of only 30 cases of multiple myeloma. With the advent of the roentgen examination, the frequency of detection of multiple myeloma increased. In the next fifteen years, 70 cases were noted, and by 1928, a compilation of the literature[14] disclosed 425 cases. This increase in number of reported cases probably does not reflect a proportionate increase in incidence but is in keeping with more frequent employment and increasing accuracy of roentgen methods.

Myelomata show an apparent predilection for males, the ratio being 3 to 1. Although occurrences among younger individuals, even children, have been reported,[7] these tumors are usually encountered between the ages of forty and sixty years. The authenticity of such a diagnosis in children has been questioned, and we may assume that, like carcinoma, multiple myeloma is essentially a disease of middle and old age. In regard to the etiology of multiple myeloma, the same theories are set forth which have long furnished ground for speculation and argument in the case of all forms of malignancy, namely, trauma, chronic irritation, or infection. Plasmocytoma is, as far as anyone now knows, an ultimately fatal malignancy.

The myelomata may arise from any of the embryonic cells in the bone marrow, the myeloblasts, myelocytes, lymphocytes, erythroblasts, and the plasma cells.[12] But, practically, all the cells may be ignored except the plasma cell. Its occurrence in multiple myeloma is the most constant. Occasionally, the myelomatous cells appear

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modified beyond differentiation, perhaps representing plasma cells in some stage of anaplasia. These atypical cells have suggested the possibility that the myelomata do not arise from the blood-forming cells but from the adventitial cells in the marrow.[12] Such an origin might partially explain the ability of the tumor to destroy bone; certainly, it would explain the aleucemic features of multiple myeloma. However, the frequent appearance of a typical plasma cell in multiple myeloma discourages the deductions in favor of another cell type.

Despite recent descriptions of a "leucemic" form of multiple myeloma,[29] the classical plasma-cell tumors (Fig. 1) do not flood the blood stream with their cells. In view of this aleucemic tendency, the search for the plasma cell in the blood stream is an arduous and impractical diagnostic means. In our cases, recognized by the roentgen ray and proved by autopsy, the usual blood examination failed to show any plasma cells. Had search for the plasma cell in the blood stream been duly prolonged, or had blood been taken on frequent occasions, perhaps the plasma cell would have been found. In this connection, it might be pointed out that cancer cells, too, have appeared in the blood of patients with cancer; yet, for the diagnosis of cancer, the profession does not look to the blood. Also, the plasma cell is not pathognomonic of multiple myeloma even when found in the blood stream, since it may also be present in infectious diseases. Its presence can only be considered a "suggestive" clue to multiple myeloma.[18]

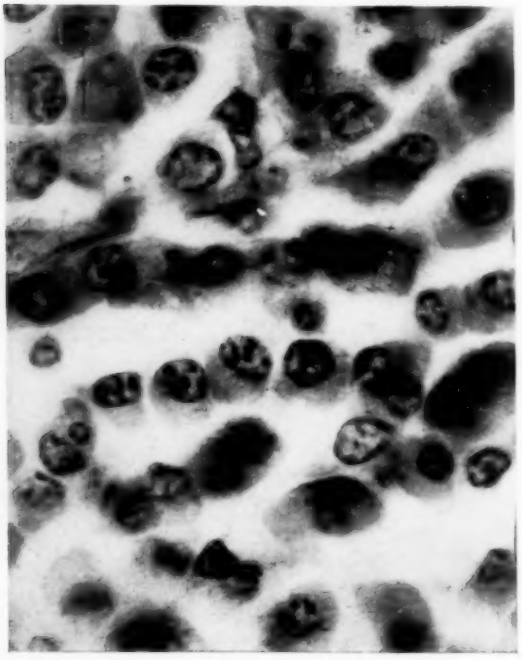

Fig. 1. Plasma cells from autopsy material. The nuclei are excentrically placed with their greatest diameter usually at right angles to the greatest diameter of the entire cell. The chromatin is arranged peripherally just within the membrane of the nucleus.

As might be expected in a tumor arising from a bone-marrow cell, plasma-cell myelomata involve most frequently and extensively those bones of greatest cancellous or red marrow content. The vertebrae, ribs, sternum, clavicles, and skull are the most commonly involved, while the long bones relatively cortical in nature are not involved with the same frequency. The tumors are represented in the roentgenogram by sharply circumscribed areas of bone destruction varying in size from that of a pea to that of an orange. As the tumors grow, pain is produced by pressure on and erosion of the periosteum, and by the pressure of the invading tumor on the adjacent nerves in the soft tissues. So far as is known, the neoplasm does not metastasize but remains locally destructive.

The absence of bone production causes the defects to have clear, punched-out edges, and renders the involved bones susceptible to fracture and deformity. Rarefaction and fracture are common in the ends of the clavicle, acromial and sternal; areas of destruction are practically always present in the ribs, with fracture, usually below the fifth rib, in 62 per cent of all cases;[14] fracture of the vertebral body is frequent at the level of the second and third lumbar with marked shortening of the spinal column. In no other disease of bone, except osteogenesis imperfecta, are "pathological" fractures so common.

While the individual tumors may be primary lesions, their widespread distribution throughout the skeletal system lends to this disease all the clinical aspects of a widespread metastasis. Pain and weakness are characteristically the most prominent symptoms. In all of our cases, there was an acute onset of pain incident to a fracture which occurred during ordinary activity. The tender spots over the bones involved corresponded to the areas of rarefaction demonstrated by roentgen examination. In one patient the tumors could be palpated. With pain as the constant symptom, other symptoms depend upon the particular bony structure suffering significant erosion. If the vertebral column is so involved, with an associated spastic paraplegia, the clinical picture can resemble an irritative cord lesion; erosion of the inner table of the skull may simulate brain tumor, or the fracture of a rib with subpleural invasion may have all the signs of a hemothorax, pleurisy or even empyema.

Radiation therapy has not been known to check the progress of the disease. Although the statement has been made that irradiation has been effective[16] in some instances, the preponderance of evidence and opinion gainsay this. However, radiation therapy has served to allay the pain associated with the rarefied and fractured bones.

In the evaluation of diagnostic measures we must consider the clinical manifestations, roentgen findings, blood changes and, as a last resort, microscopic section of the tumor tissue. The following cardinal criteria constitute the most reliable basis for a diagnosis of multiple myeloma:

1. Clinically, the history of acute (or, less commonly,—gradual) onset of pain in the bones of the trunk; a chronic nephritis, without increased blood pressure or retention of non-protein nitrogen; the finding of Bence-Jones[6] protein; a progressive anemia.

2. In the roentgenogram, the widespread distribution of multiple, sharply circumscribed defects in the marrow cavities of the bones of the trunk with high incidence of pathological fracture and deformity (Fig. 2).

Although Bence-Jones protein in the urine has long been identified with multiple myeloma, it is not found constantly, nor is its finding pathognomonic of multiple myeloma. But since it occurs less frequently in metastatic carcinoma, nephritis, leucemia, and other cachectic conditions, such appearance in the urine or blood serum is highly suggestive of multiple myeloma. Possibly Bence-Jones protein originates from the action of tumor-cell enzymes on the protein of the blood, or it may be derived from the elastin of bone tissue absorbed by tumors. Bence-Jones protein is present whenever marked destruction of bone marrow occurs. There is a diversity of opinion as to the frequency of its occurrence in multiple myeloma. However, more than 50 per cent of cases show Bence-Jones

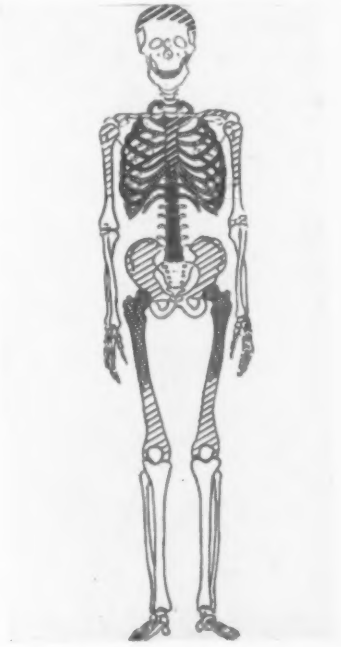

Fig. 2. Incidence of skeletal involvement according to location. The solid black area indicates the site of most frequent involvement; the heavy diagonal lines, the common sites; checked areas, the fairly common sites; light diagonal lines, the occasional sites, and the white areas, rare sites. (After Geschickter and Copeland.)

protein upon search, after multiple myeloma is considered clinically and roentgenologically. The finding is of strong corroborative importance, but no more than that.

The blood protein concentration is of interest. The Bence-Jones protein in the blood may give rise to a hyperproteinemia of the globulin type. In a series of 241 blood protein determinations made on patients with many kinds of disease, one case of multiple myeloma showed the highest content.[28] On the other hand, normal and low globulin values have also been reported in this condition.[17] The low globulin values might be explained on the basis of profuse excretion of Bence-Jones protein in the urine rather than retention in the blood. In the case of hyperproteinemia, Bence-Jones protein was with difficulty demonstrable in the urine, while those with low globulin values were actively excreting the substance in the urine. Further research along these lines will undoubtedly warrant more specific conclusions.

The blood picture is not distinctive in multiple myeloma. There is an anemia associated with the malignant course of the disease, which, though essentially of secondary type, may resemble the primary form by reason of the extensive destruction of the bone marrow by the tumors. In uncomplicated cases, the leucocyte count is within normal limits. Plasma cells, as we have said above, are not easily found.

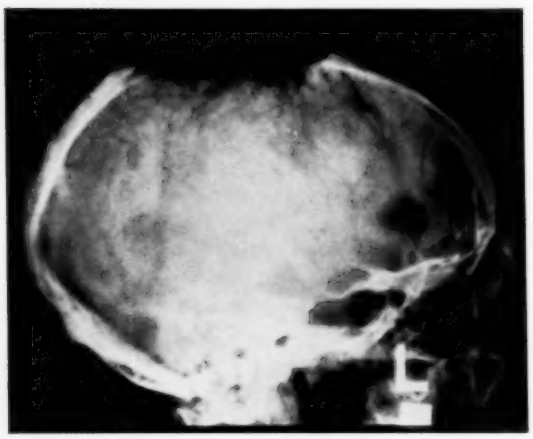

Fig. 3. Case 1. Roentgenogram of skull showing large defects of myeloma in the calvarium.

In those cases showing only a single lesion of bone, or with an entirely extraskeletal tumor (classed incongruously, in our opinion, as multiple myeloma), the diagnostic features just discussed do not obtain. These so-termed myelomata are related to the true plasma-cell myelomatosis only in the matter of the plasma cell which is common to both. The diagnosis is rarely to be made without the demonstration of the plasma cell in the microscopic section. Such cases are hence deleted from the series under consideration.

Two illustrative cases are presented in detail and a compilation of the series from the University Hospital follows:

Case 1. W.T., #255598, white male, aged sixty. Chief complaint, "pain and fractures." Five years before admission the patient noticed a tender spot on one of his right lower ribs. About a year later, nodules appeared on his head. He was told elsewhere that he had "sarcoma" and periodically reported for roentgen treatment. Subsequently, other masses appeared, and within the following year, he heard both clavicles "crack" while doing ordinary lifting. Some short time after this, his left hip fractured spontaneously while he was walking. He noticed a progressive loss of strength.

On admission, examination revealed a soft tumor measuring about 4″×5″ at the cranial vertex (Fig. 3). An irregular border, presumably the edge of the eroded skull, could be palpated about the mass. In the forehead there was another such lump, smaller, but which also had a sharp hard border suggesting an erosion of the skull. On the eighth right rib, in the midaxillary line, there was a tender, nodular mass apparently attached to the rib. The spine showed limitation of motion in all directions. Blood pressure, 135/70.

Laboratory examination. Urine, albumin +++; Bence-Jones protein present. Erythrocytes, 2,130,000; leucocytes 9,700; hemoglobin, 38 per cent; color index, 0.9. The red cells were distorted and of "pencil type." No plasma cells were found.

Roentgen studies demonstrated old, healed fractures of both clavicles; marked destruction of the left scapula and humerus; old fractures

of 4th and 5th ribs, right, with destructive changes in the 7th, 8th, and 9th (Fig. 4); defects in the skull and pelvis. Areas of rarefaction as small as a bean and as large as a lemon were visualized. There was no evidence of any bone production, the lesions being clearly outlined, with the "punched-out" appearance so typical of this disease.

FIG. 4. Case I. Roentgenogram showing the rarefied areas in the clavicles, with fracture of the left clavicle, and rarefied areas in the ribs.

The patient became progressively weaker and died within two months. At autopsy, widespread infiltration of the bone marrow with plasma-cell myeloma was observed in the sternum, vertebrae, and all of the ribs, in addition to the sites previously recognized by the roentgen ray.

CASE II. C.M., #254171, white male, aged fifty-six. Chief complaint, "pain in the back and over the ribs." Three months before admission, while the patient was pushing upward on a large wrench with his elbow against his ribs, something "gave way" in his chest. The pain was severe and constant. Two weeks later, similar pain developed in his back and remained there constantly, although varying in degree. While lifting a heavy object from the ground, he noticed a sharp pain in the right rib margin. On the night prior to admission, a sharp pain developed over the heart and the patient heard something snap when he coughed. He gave a history of progressively increasing weakness.

On admission, examination revealed a tender area about the size of a silver dollar over the 7th rib, left. Also, the right costal margin was tender. The spine was completely immobile in the region of the lumbosacral articulation. Thumping produced pain, as did attempted flexion of the spinal column. Blood pressure, 120/62.

Laboratory examination. Urine, albumin++; Bence-Jones protein present. Erythrocytes,

FIG. 5. Case II. Roentgenogram showing typical defects of multiple myeloma throughout the cranial vault.

3,420,000; leucocytes, 8,700; hemoglobin, 74 per cent; color index, 1.1. No plasma cells were found. Non-protein nitrogen, 34 mg. per 100 c.c.

Roentgen studies demonstrated disseminated focal areas of rarefaction involving the pelvis, lumbar spine, ribs, skull (Fig. 5), femora, and humeri. The individual defects were circular and sharply defined.

During his period of hospitalization, the patient failed rapidly. The pains of which he complained increased in severity until his death, three weeks after admission. Autopsy disclosed myelomatous involvement of skull, ribs, vertebrae and femora. Plasma cells were demonstrated in the lesions.

These cases present the early pain, the characteristic pathological fractures induced by ordinary activity, the multiple bony defects with striking absence of oste-

ophytic proliferative reaction, the chronic nephritis without hypertension or increased non-protein nitrogen, the presence of Bence-Jones protein in the urine, the secondary anemia, the apparent absence of plasma cells in the blood, and the progressive debilitating nature of the disease.

In the autopsy records of the University Hospital from 1896 to 1931, five cases of multiple myeloma are to be found among 3,700 autopsies. In addition to these, the hospital clinical records list 8 additional cases since 1926, four of which are well authenticated. Post-mortem and clinical records therefore combine to provide a total of 9 proved cases.

Of the 4 cases with questionable diagnosis, 3 lack both clinical and roentgen criteria of multiple myeloma and have obviously been erroneously classified. The fourth instance, however, possesses a clinical picture compatible with this disease but the roentgen findings lack essential details. Multiple defects are present in the skull of this patient, but none in the vertebral column or ribs. Further, the lesions in the skull are somewhat irregular in outline with slight, but none the less definite, evidence of associated bone production. The spontaneous recovery of this patient from an almost moribund state adds weight to the assumption that the lesions may have been those of syphilis. The patient was thirty-nine years old.

Some years ago, it was declared that the diagnosis of multiple myeloma from the roentgen examination alone was exceedingly rare and difficult, if not impossible.[3] Since that declaration, however, many illuminating cases of multiple myeloma, with special emphasis on the roentgen aspects, have been reported. At the present time the value of the roentgen examination in the diagnosis of multiple myeloma is widely acknowledged. In the cases reported, the roentgen findings either indicated or confirmed the diagnosis.

In the roentgenologic differentiation of multiple myeloma from other disseminated osteolytic diseases, occasional confusion may arise in connection with widespread osteolytic metastasis of carcinoma in those patients where no primary tumor can be discovered (Figs. 6 and 7). In his "Röntgendiagnostik," Assmann states, "In many cases, a definite differentiation is not possible on the roentgenogram alone, between osteoclastic carcinoma metastases and multiple myeloma; but, to be sure, the transparencies or defects in multiple myeloma are usually more sharply defined."

Fig. 6. Roentgenogram showing the metastatic lesions of carcinoma with fuzzy irregular borders.

Usually, the carcinomatous metastases are not so extensively distributed, and are located close to the entrance of the nutrient artery. Metastases to the skeletal system frequently involve the spine, but usually show some bone production. Lacking this bone production, the spine can be so rarefied in multiple myeloma that the vertebral bodies are distinguished only with difficulty from the intervertebral discs. Also, the spine involved by metastases is less frequently deformed by fracture and gross shortening. Furthermore, the ribs, uncommonly involved by metastases except from

a primary neoplasm of the cervix uteri or by direct extension from breast carcinoma, are the most constantly involved in multiple myeloma.

Other diseases sometimes to be considered in the differential diagnosis are:

1. *Osteomalacia*, which usually occurs in pregnant women and never shows rarefaction in the cranial bones. The absorption of calcium salts is diffuse, whereas the rarefactions in multiple myeloma are localized.

Fig. 7. Case 1. The lesions of multiple myeloma, more sharply defined.

Deformities in osteomalacia are due to bending of the softened bones, but in multiple myeloma the deformities are due to poor alinement of true fractures.

2. *Endothelioma*, when multiple, may be confused with multiple myeloma because of the similar distribution in ribs, vertebrae, skull, and cancellous portions of the long bones.[12] It can be distinguished, nevertheless, from the radioresistant multiple myeloma in its sharp initial response to irradiation. Further, endothelioma more commonly occurs in younger individuals.

3. *Paget's disease*, or osteitis deformans, as a fibrotic degeneration of bone with subsequent recalcification, shows in the degenerated areas diffuse striations and trabeculations with new bone formation. This reformation of bone is never observed in multiple myeloma.

4. *Syphilis*, in the form of disseminated lesions, always shows soft tissue reaction and adjacent bone production.

5. *Lymphosarcoma of bone*, although extremely rare, might be confused with multiple myeloma in the similar distribution. However, the individual tumors are more irregular and lack the "punched-out" appearance of multiple myeloma.

6. *Chloroma* and multiple myeloma are considered to fall in the same category.[33] The microscopic findings are similar, namely, a predominance of a form of plasma cell in the lesions. The roentgen findings are also similar. Grossly, the sectioned chloroma presents a characteristic, iridescent greenish color, while the myeloma is red; also, in chloroma, sternal and substernal involvement is extensive. Chloroma occurs in younger individuals and is associated with a leucemia.

CONCLUSIONS

1. Except for the microscopic study of biopsy material, no one diagnostic procedure is infallible in the recognition of multiple myeloma.

2. Comprehensive roentgen studies of the bone lesions offer a reliable group of signs typical of this disease. Such studies have in recent years contributed greatly to the increase in the number of authenticated cases appearing in the literature.

3. The history of illness, blood and urine findings and the clinical course of the disease corroborate but scarcely rival the roentgen findings in importance.

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THE PERSISTENCE OF CARCINOMA IN THE CERVIX UTERI AFTER IRRADIATION*

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MEDICAL literature abounds with statistics regarding the relative merits of radical surgery and radium in the treatment of carcinoma of the cervix uteri. At present there is little use for such comparisons, for the merits of radium have been amply demonstrated both as a curative and a palliative measure. Discussion of radium *versus* surgery should be abandoned. With our present knowledge the pertinent question is, shall we confine the treatment of cervical cancer to radium alone? Should not radical surgery be employed in conjunction with radium for operable cases, reserving radium alone for patients with more advanced growths? The present investigation deals with one phase of this important question; it is a pathologic study of a number of uteri removed by radical operation after preliminary irradiation by accepted methods.

STATISTICS

Comparisons of the results obtained by surgery alone with those reported for radium therapy show in general that the figures are much alike—20 to 25 per cent cures of all cases presenting themselves for treatment, 40 to 50 per cent cures of so-called operable cases (falling in Groups I and II of Schmitz's classification).

Absolute cures	20 to 25%
Cures in operable group	40 to 50%

However, it must be appreciated that statistical comparisons contain many inaccuracies. Detailed discussion would take us too far afield, but the more glaring sources of error should be mentioned. In comparing absolute cures, figures are reliable only if the material presenting itself at the various clinics is identical, i.e., contains the same relative proportions of early, borderline, and late cases. If the material is not equal, serious errors may occur: for example, if Dr. *A* has only 25 per cent of advanced cases (Group IV), from which no cures can be expected, and Dr. *B* has 50 per cent, it is evident that Dr. *A* will have better results than Dr. *B*. Such differences in material do occur: Lynch[14] reports 26.6 per cent of Group IV from this clinic, whereas Ward[24] reports only 4.4 per cent of Group IV from the Woman's Hospital in New York.

Reliable comparisons in the operable groups are most difficult because they depend upon individual opinion as to the proper classing of cases as operable or inoperable. What one man thinks is an operable case another may not. Uniform agreement may be had only in the very earliest and the most advanced. Variation in individual opinion is most striking when we compare the figures reported by a number of surgeons with those from radiologists. Table I was compiled to illustrate this point; it shows that on the average the operability rate reported by the surgeons is some 40 per cent greater than that reported by the radiologists. No doubt some real difference in material existed, for more early cases, fewer advanced ones, gain admittance to purely surgical clinics, whereas the reverse is true for radiologic clinics; but real difference in material could hardly have been as great as 40 per cent. Surgeons have had to depend upon their operative efforts for their cures; they have naturally inclined to consider as operable more cases than have radiologists, who have leaned in the opposite direction in order to be certain that no borderline cases have been classed in their operable groups.

These two important considerations

* Read at the Seventeenth Annual Meeting, American Radium Society, New Orleans, La., May 9–10, 1932.

must be borne in mind when judging statistical comparisons of results obtained by radium and surgery. The error pointed out for comparisons of cures in the operable groups would seem to indicate that the possibility of cure by surgery is far greater than that by radium if surgeons should select their cases as carefully as do the radiologists.

Table I[2]

ILLUSTRATING THE MARKED DIFFERENCE IN OPERABILITY REPORTED BY SURGEONS AND RADIOLOGISTS

		Proportion of cases operable, in per cent	
Surgeons	Franz	81	
	Bonney	63	
	Wertheim	46	
	Stoeckel	70	
	Bumm	68	
	Zweifel	58	Av. 64.3
Radiologists	Ward	25.9	
	Heyman	39	
	Regaud	18.3	
	Healy	24.5	Av. 26.9

PATHOLOGY

The present study approaches the problem differently. Statistics tell us of cures, they are unable to tell us why a much larger proportion of early cases are *not* cured. Only pathologic study can answer this question.

In regard to surgery, pathologic study has already furnished an answer; in a word, cases in which no cure resulted were not operable after all, cancer had extended beyond the cervix, either as metastasis or direct extension. Clinically, when the growth seems to be confined to the cervix or immediately adjacent vaginal mucosa, without fixation of the cervix or only slight induration in the parametria, it is considered operable. The term needs re-defining for technical removability should not determine operability. No cure can be expected when cancer has extended beyond the cervix, even microscopically. Martzloff,[15] in his pathologic study of the specimens removed by radical operation at the Johns Hopkins Hospital, found cancer in the parametrium 120 times; not one of these women lived five years. In a small way we have been able to make a similar observation. Of 18 uteri removed by a Wertheim operation, cancer was found in the parametrium in 7. All 7 of these women died in less than five years. The other 11 are alive and well from five to fifteen years. These facts confirm pathologically what statistics have suggested—that surgeons have operated upon cases which were really inoperable and therefore not susceptible of surgical cure.

With radiation therapy alone there is less opportunity to check the clinical grouping. The plan of treatment at the University of California Hospital under the direction of Dr. Frank W. Lynch, has afforded an opportunity of examining a number of uteri from cases irradiated then operated upon. This has enabled us to draw some conclusions regarding the efficacy of irradiation in operable cases. All women with cervical cancer were treated by radium irradiation; those in which the growth appeared to be confined to the cervix were later subjected to the Wertheim operation.

Table II

AMOUNT OF RADIATION EMPLOYED

	No. of cases	Amount of radiation
1916–1921	18	None preoperatively.
1921–1927	11	Single large dose in canal; e.g., 2,200, 4,000, 1,867, 2,329, 3,197, 2,290, 750 mc-hr.
1927–1931	11	Stockholm method; e.g., 3,777, 3,989, 5,286, 3,413, 5,008, 2,528, 4,139, 3,815 mc-hr.

The series was started in 1916; for the first five years radium was not used before operation. In the next 11 cases a single large dose was given in the cervical canal (2,400 mc-hr.), occasionally supplemented by a small dose applied against the cervix, or by radon seeds. Since that time the technique has been patterned after that in

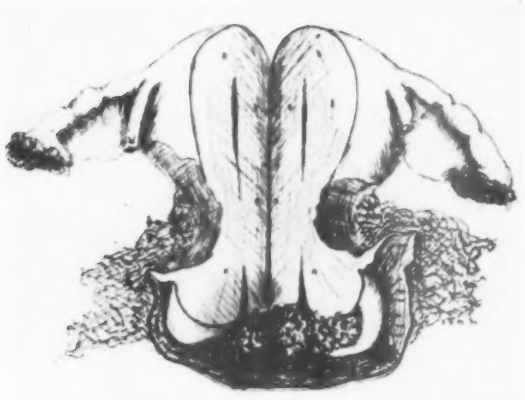

Fig. 1*a*. Case M.H. Everting growth. Group I. Irradiation: single large dose, 2,486 mc-hr., plus needling, 711 mc-hr.; total dose, 3,197 mc-hr. Operation thirty-seven days later. One of three specimens showing cancer remaining grossly after irradiation. For microscopic findings see Figure 1*b*.

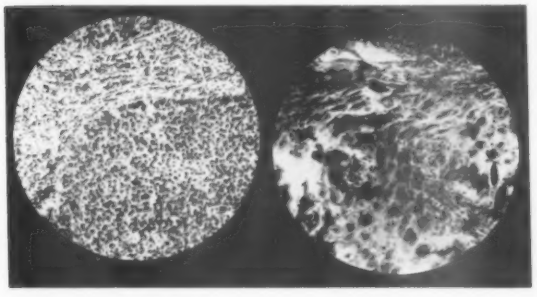

Fig. 1*b*. Cervical sections of specimen shown in Figure 1*a*. On the left is the appearance of the cancer cells at biopsy before any treatment. On the right is the appearance after irradiation and operation. Although the cells have been markedly changed by irradiation, it is noteworthy that this is one of the cases in which cancer remained grossly thirty-seven days afterward. Patient alive and well over five years.

vogue at the Radiumhemmet in Stockholm, except that slightly smaller doses have been given in the cervical canal. The object of preoperative irradiation has been the cleaning up of the local sloughing ulceration, the blocking of lymphatics, and the checking of the growth, but not necessarily complete eradication of the disease. By preventing peritonitis this preparation has done much to make operation safer. The fibrous replacement incident to irradiation adds to the technical difficulty by destroying normal planes of cleavage, but the increased safety far outweighs this disadvantage.

MATERIAL

Forty specimens were examined, all originally classed as operable (Groups I and II); 22 had been irradiated preoperatively and 18 had not. Careful gross and microscopic examinations were carried out. Although no attempt was made to cut serial sections,

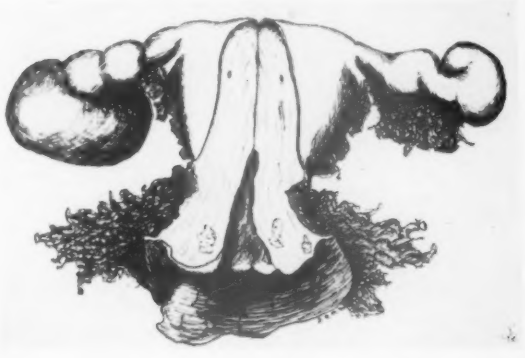

Fig. 2*a*. Case O.D. Everting growth. Group II. Irradiation: Stockholm technique, 3,989 mc-hr. Operation twenty-five days later. No clinical evidence of cancer remains after irradiation. This patient also had regional gland metastasis; died seven months after operation of recurrent cancer. For microscopic findings see Figure 2*b*.

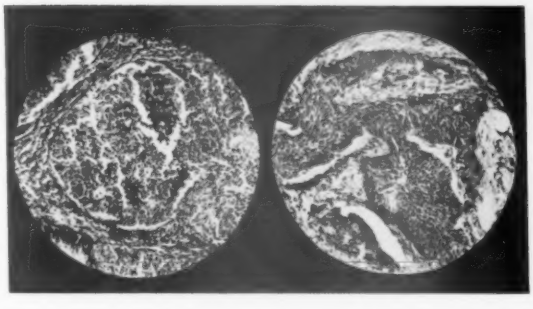

Fig. 2*b*. Cervical sections from specimen shown in Figure 2*a*. On the left is the appearance at biopsy before irradiation. On the right is the appearance after irradiation and operation; these cells are interpreted as being alive. This case illustrates how deceiving immediate clinical response to irradiation may be; grossly no cancer remains in the cervix, microscopically it does. The patient would probably have had a recurrence, even if no metastasis had existed at the time of operation.

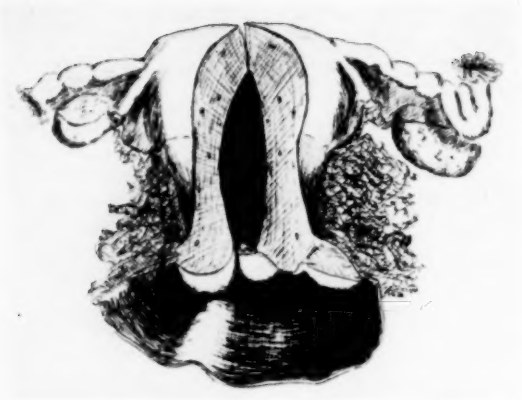

Fig. 3*a*. Case R.H. Everting growth. Group I. Irradiation: Stockholm technique, 3,795 mc-hr. Operation nineteen days later. No gross clinical evidence of cancer remains after irradiation. Patient alive and well over five years. For microscopic findings see Figure 3*b*.

Fig. 4*a*. Case E.E. Inverting growth. Group II. Irradiation: single large dose in cervical canal, 2,640 mc-hr. plus needling 1,064 mc-hr.; total, 3,704 mc-hr. Operation thirty days later. No clinical evidence of cancer remained because of the inverting type of growth. For microscopic findings see Figure 4*b*.

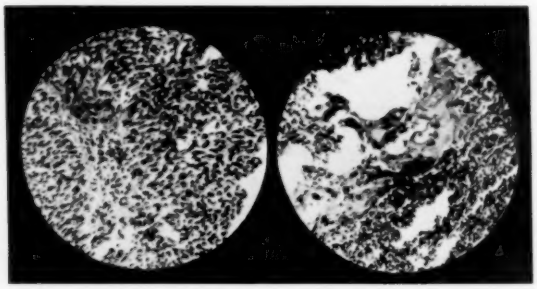

Fig. 3*b*. Cervical sections of specimen shown in Figure 3*a*. On the left is the appearance at biopsy, before irradiation. On the right is the appearance after irradiation and operation. A few epithelial remnants remain. This section is shown to illustrate the sort of reaction interpreted as "only a few dead cells remaining."

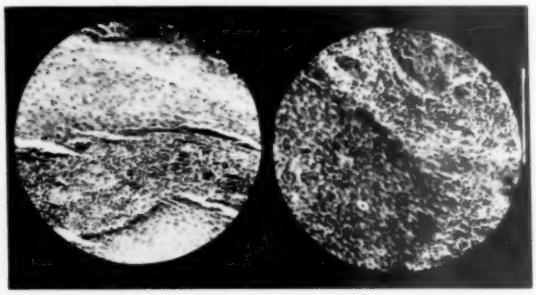

Fig. 4*b*. Cervical sections from specimen shown in Figure 4*a*. On the left is the appearance of the cancer cells at biopsy, before irradiation. On the right is the appearance after irradiation and operation; these cells are interpreted as being alive. This case again illustrates how deceiving immediate response to irradiation may be.

blocks were taken from all suspicious or significant areas. Therefore positive results are positive, negative results may be open to question. Observations upon this material aid us in answering the question of why radium may fail to cure the early case. They bring out the significant fact that many cases may be insufficiently or improperly irradiated without our knowledge.

In 10 of the 22 irradiated specimens evidence of live cancer was found. Some of the cells interpreted as being alive showed granular and hydropic changes. Other

Table III

Outline of Material

	No Preoperative Radium	Preoperative Radium
Specimens examined	18	22
Live cancer in cervix after operation		
Dead or dying cells in cervix after operation		3
No evidence of cancer in cervix after operation		9

Fig. 5*a*. Case M.S. Everting growth. Group II. Irradiation: Stockholm technique, 3,291 mc-hr. Operation eleven days later. No clinical evidence of cancer remains after irradiation. For microscopic findings see Figures 5*b* and 5*c*.

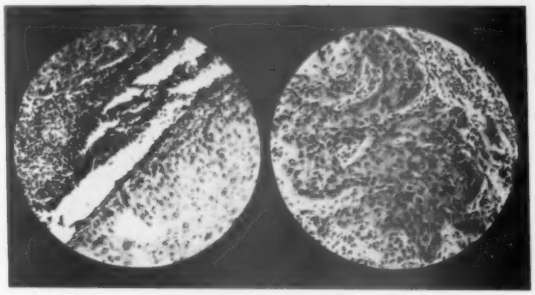

Fig. 5*b*. Cervical sections from specimen shown in Figure 5*a*. On the left is the appearance at biopsy; on the right, after irradiation and operation. Clinically no cancer remains after irradiation; microscopically it does.

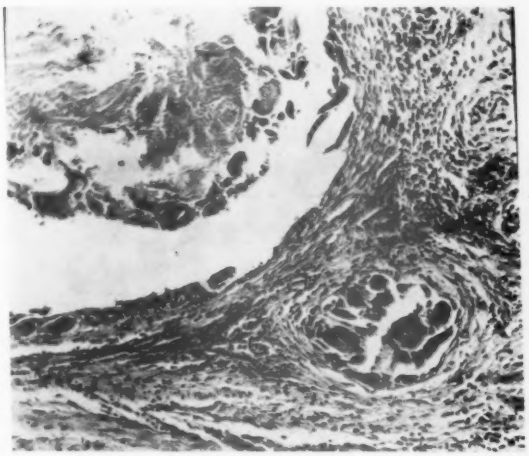

Fig. 5*c*. Photomicrograph of section taken through left parametrium. Dead cancer is seen in the lymph spaces. The patient died in seven months of recurrent cancer. This case further illustrates how gloomy is the prognosis when cancer has extended beyond the cervix, even though it is apparently destroyed by irradiation.

portions of these cervices showed distinctly degenerated cell masses, plasma and round cell infiltration, and beginning fibrosis. Three specimens showed a few dead cancer cells. The other 9 cervices revealed no evidence of cancer, but did show varying degrees of tissue repair. The presumption is that 12, possibly only 9, of these 22 women could have escaped recurrence had not operation been performed.

The evolution of the changes in cancer incident to irradiation have been studied by Ewing,[6,7] Alter,[1] Norris and Rothschild,[18] Farrar,[8] Dyroff,[5] and others. There is first a specific action upon the cancer cells, probably destroying their powers of reproduction, later the more differentiated stroma is stimulated to the formation of new connective tissue with eventual fibrosis. Some time is required for the cancer cells to disintegrate and be removed. This period varies with the resistance of the particular cell type and the dose of radium. While examples are cited of the complete disappearance of cancer within a few days after mild irradiation, small growths may persist in spite of the most intensive treatment. Generally speaking, by the end of the second week after irradiation, cells which are going to die show marked changes, such as swelling or breaking up of the nuclei, liquefaction necrosis, fusion into giant cells. It was the absence of such changes in some portion of the cancers examined which led me to say that the cells were alive. Undoubtedly they must have been hurt, for they showed distinct microscopic differences from their appearance at biopsy.

TIME FACTOR

Attempt was made to analyze the findings with reference to the intervals of time

elapsing between irradiation and operation. No definite relationship could be determined. The majority of operations were performed two to five weeks after the last radium treatment. The shortest interval was ten days; despite diligent search no evidence of cancer could be found in this specimen. The longest interval was 165 days; a few dead cancer cells were found in the cervix of this specimen.

TABLE IV

INFLUENCE ON PATHOLOGIC FINDINGS OF TIME ELAPSING BETWEEN RADIATION AND OPERATION

No Definite Relation	Comment
Longest interval..... 165 days	Dead cancer cells in pecimen.
Shortest interval..... 10 days	No microscopic evidence of cancer.
Majority..... 2 to 5 weeks	

On the basis of the studies mentioned, it would appear that enough time had elapsed between irradiation and operation for the cancer cells to be either entirely destroyed or at least to show such marked degenerative changes that no mistake could be made as to their non-viable appearance, if such response were going to occur at all.

TABLE V

GROSS REACTION OF CERVIX TO IRRADIATION MAY BE DECEIVING

Number of cases examined after preoperative irradiation	22
Clinical evidence of cancer	3
Pathologic evidence of cancer	13

These observations simply mean that the immediate clinical result may be an unreliable means of judging whether or not a cure is to be anticipated, although it is almost our sole criterion.

DISTRIBUTION OF DOSAGE

Further analysis showed that there was some relationship between the persistence of cancer and the distribution of radium dosage between the canal and the vaginal surface of the cervix. It became clear that at least a moderately large dose must be given in the canal to obtain the destruction of all cancer cells.

Of the 11 cases in which the greater part of the irradiation was confined to the vaginal surface of the cervix, 8 showed some evidence of cancer remaining—only dead cells in 2 instances; of 7 cases which received less than 800 mc-hr. in the canal 6 showed cancer remaining, although again only dead cells were present in 2. The incidence of the persistence of cancer after thorough irradiation of the canal was less.

TABLE VI

INFLUENCE OF DISTRIBUTION OF RADIUM BETWEEN CANAL AND VAGINAL SURFACE OF CERVIX

		Cells Alive	Cells Dead	No Cancer
11 cases (all or most in canal)	Cancer in cervix	4	1	6
11 cases (most in vagina)	Cancer in cervix	6	2	3
7 cases (less than 800 mc-hr. in canal)	Cancer in cervix	4	2	1

CLINICAL FINDINGS

The recorded pelvic examinations of these 22 women, made just prior to operation, were carefully studied in order to ascertain whether or not there was clinical evidence of the persistence of cancer after irradiation. In 3 instances, such evidence was present, and had not operation been planned, further irradiation would have been carried out. Microscopically, there was evidence of cancer in 13.

It is clear that these cases did not receive adequate irradiation, or that dosage was improperly distributed. They are of serious import for two reasons: first, because of the *absence* of clinical evidence of cancer after irradiation in all except 3, while cancer was found microscopically in 13; secondly, because the method of irradiation employed was roughly equivalent to those in use else-

where, having given a 38 per cent five-year cure in a series of similar cases (Groups I and II) which were irradiated in essentially identical fashion, but were not operated upon for one reason or another.

PARAMETRIAL INVOLVEMENT

Recurrence in cases adjudged early may occur because of cancer in the parametrium, not appreciable on pelvic examination; radium may fail to kill it, as it may fail in the cervix. Cancer was found in the parametrium in 4 of these 22 specimens, markedly degenerated in 2, apparently alive in the other 2. In a fifth case metastasis to a regional lymph gland was demonstrated, making an incidence of 18.2 per cent for extension beyond the confines of the cervix, a figure which might also be taken to represent error in diagnosis of operability. The incidence for the non-irradiated group was 38.9 per cent. The difference in percentages

Table VII

SERIOUSNESS OF PARAMETRIAL EXTENSION

Incidence of extension	Non-irradiated group	38.9%
Incidence of extension	Irradiated group	18.2%
		Comment
Live cancer in parametrium	2	1—alive 7 yr. Probable recurrence. 1—alive 4 yr. Metastases in lung.
Dead or altered cells parametrium	2	1—dead of cancer in 7 months. 1—alive 1 yr. Probable recurrence.
Cancer in gland	1	Died in 6 months of recurrent cancer.

might be due to the greater liberality in diagnosing operability when surgery alone was employed, or to irradiation. Table VII shows how gloomy is the prognosis in such cases, even though the cancer has apparently been destroyed by radium.

LITERATURE

Several observers have reported inability to find cancer in specimens from women irradiated, then operated upon. Many of the details were lacking; however, 22 such cases were collected. These observations are summarized in Table VIII.

Table VIII

UNABLE TO FIND CANCER AFTER IRRADIATION

Observer	Cases	Interval	Dose
Ward[23]	3	3 yr., 2 mo., 6 mo.	2,400 mg-hr. in canal
Ewing[6,7]	2	4 wk., 6 wk.	
Schauta[20]	8	—	—
Schmitz[21]	7	—	—
Schmidt	2	—	—

On the other hand, Monod[17] reported the finding of cancer in the cervix in 15 of 74 cases irradiated five to six weeks before operation. Mayer[16] found cancer in 60 of 72 uteri irradiated six weeks before operation, but his dosage was small, only 1,200 mc-hr., employed merely as preparation for operation. The most interesting and detailed reports come from Lahm,[12,13] 8 cases in 1928, 18 in 1930. Twenty-four were either distinctly operable, or at most borderline when first seen. They received from 3,600 to 4,100 mg-hr., and practically all were treated with deep roentgen therapy as well. Examination of these specimens revealed no evidence of cancer in 6, cancer cells in various stages of degeneration in 11 (he considers them dead), and "fresh cancer" in 7 (new cancer which had grown after the destruction of the original growth by irradiation). It is far more likely that the "fresh cancer" simply represented portions of the original growth which had not been destroyed by irradiation. However his thought brings up the question of "bad soil"; some late recurrences may be on the basis of new cancer arising in "bad soil." In my own cases and those reported by Monod, Mayer, and Lahm, the time elapsing between irradiation and operation was too short to make such an explanation likely.

TABLE IX

FOUND CANCER AFTER IRRADIATION

Observer	Cases	Interval	Dose
Monod	15 of 74	5 to 6 weeks	Regaud method.
Mayer	60 of 72	6 weeks	1,200 mc-hr.
Lahm	No cancer in 6; degen. ca. 11; "fresh ca." 7	4 to 8 weeks	3,600 to 4,100 mc-hr. (plus x-ray)
Morton	No cancer 9 Dead cancer 3 Live cancer 10	2 to 5 weeks	2,000 to 5,000 mc-hr.

CLINICAL COROLLARY

In Lynch's[14] latest paper dealing with this series of cervical cancers he arranged the material in curves to show the number of survivors at various periods of time after irradiation (no operation), and noted a marked drop in the composite curve for Groups I and II after three years. In the light of these findings, it seems likely that the drop was caused by the return of cancer which had been badly injured but not killed by irradiation, although the growth of an entirely new cancer cannot be excluded (Chart 1).

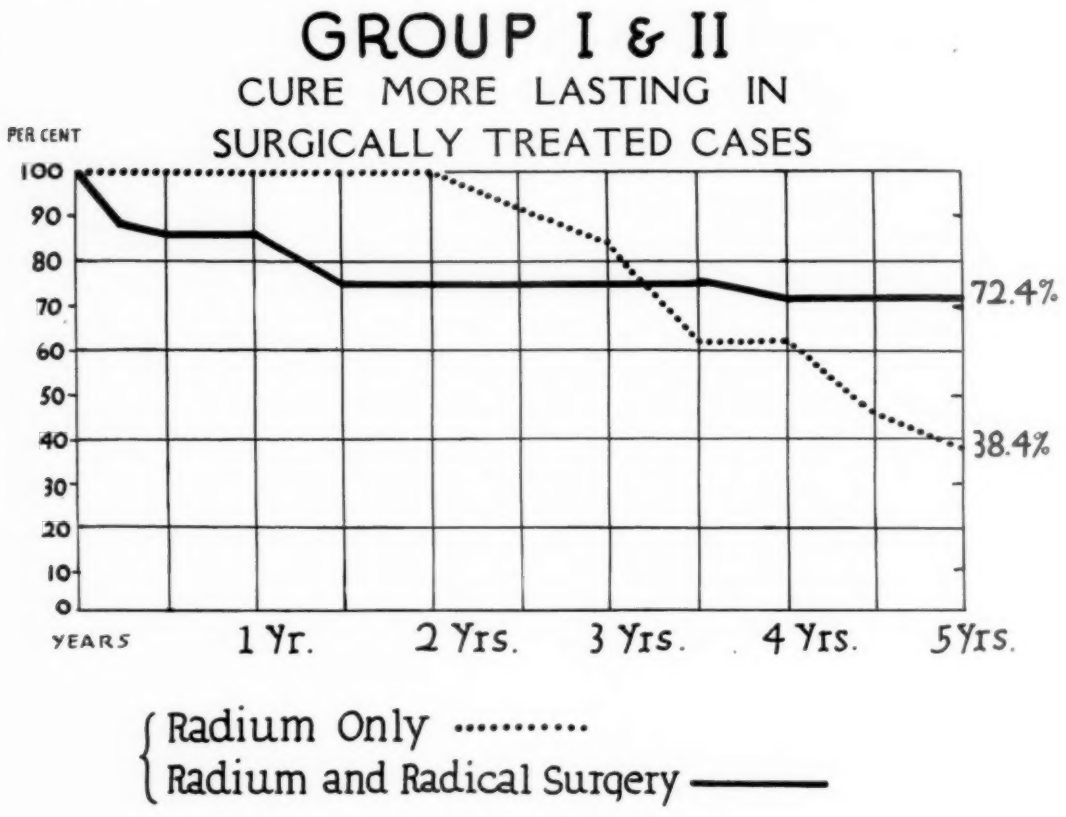

CHART I

COMMENT

Finding cancer in the cervices of approximately 50 per cent of Groups I and II cases after irradiation only serves to draw our attention more closely to our treatment of these cases. If irradiation alone is to be em-

ployed, more progress will have to be made in the technique of its application. A combination of irradiation and surgery should theoretically be an improvement over irradiation alone in that residues of cancer, injured but not dead, would be removed. As a matter of fact, the combined treatment in this clinic has given a 70 per cent cure in the operable groups, as compared with 38 per cent where irradiation alone was employed.

Borderline cases are undoubtedly best handled by radiation therapy, for surgery is of no avail when cancer has extended beyond the limits of the cervix, except in rare instances. With irradiation there is a small salvage.

Radium should cure the Group I case, and does in many instances. But, practically speaking, there are many difficulties in the way of a confident diagnosis of Group I. The inverting growth particularly may deceive the observer. If the growth is more extensive than appears upon the surface, irradiation fails to effect a cure in a certain proportion, but, in any event, furnishes ideal preparation for subsequent operation. More careful selection of cases suitable for operation will do much to lessen primary mortality, and will *assure* the vast majority of these women of permanent cure.

A possible partial explanation for insufficient irradiation suggested itself: irradiation as well as exerting a specific action on malignant cells causes marked contraction and fibrosis. Many older observers have speculated that perhaps this was its most important effect, in blockading and choking off nests of carcinoma cells. Perhaps it has its drawbacks also; may it not in some degree protect the malignant cells? May it not by contraction and scarring make parts of the growth inaccessible to irradiation, particularly when divided dosage is spread over any considerable period of time? The desirability of irradiating the canal thoroughly has been demonstrated; actually it is often found impossible to do so. Sometimes this condition exists primarily, but more often it is due to the changes incident to irradiation.

This possibility and the immediate favorable reaction to irradiation so often deceptive, are problems of radiation therapy which will always require serious thought.

CONCLUSIONS

Recurrence occurs in approximately 50 per cent of Group I and II cases (operable cases) treated by irradiation.

Recurrence is probably due to the persistence of live cancer cells in the cervix in a large proportion of these cases.

The gross reaction of the cervix is not a reliable index of the adequacy of irradiation.

It is premature to discard surgery from consideration in the treatment of truly early cases.

Employing a combination of irradiation and surgery 67.8 per cent of operable cases have been cured for more than five years.*

* For discussion see page 520.

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BENIGN UTERINE HEMORRHAGE: ITS TREATMENT WITH RADIUM*

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THIS study is concerned with the treatment of simple menorrhagia with radium, the indications for treatment, the technique employed, and the results. This is one field in which treatment by radium is of the greatest value, and with proper judgment in the selection of patients and with careful technique, the results often surpass those of any other form of treatment. It is interesting to note that this is the first pelvic condition in which radium was applied as a therapeutic agent, if our knowledge is correct, and the trial was carried out in France, the birthplace of knowledge of the element. In 1906 Oudin and Verchère reported having treated uterine hemorrhage due to benign lesions by the introduction of 11 mg. of radium element into the uterine cavity, and allowing it to remain in place for fifteen minutes, repeating the treatment five or six times at intervals of four or five days. Filtration was not employed, except that of the glass container, and results were not happy; the beta radiation caused much local reaction, and further work was abandoned. Better results were obtained by Chéron, who used 30 mg. of radium in a glass tube, and a 0.5 mm. silver filter, placing the element within the uterine cavity or the cervical canal, and leaving it there for six to eight hours, and repeating this procedure several times at intervals of a few weeks, for a total dosage of 2,160 mg-hr. In his report before the Académie de Médécine in 1909 he gave results with 120 women suffering from small uterine myomas; amenorrhea resulted in 117, and shrinkage of the tumor in 108. In 1914, Gauss and Krinski reported excellent results in 30 cases in which treatment was with mesothorium applied in the vagina or cervix, and stated that the results were more rapid than could be obtained by roentgen rays.

In this country, Abbé[1] in 1906 reported treating one patient with radium, and later reported two good results[2] with fibroid tumors, in one case of which treatment was given in 1905, and in one in 1909. There were then many scattered reports of results, culminating in the paper of Kelly and Burnam, in 1914. They reported excellent results in 39 cases of benign uterine bleeding; 21 of the patients had fibroid tumors of medium or large size. Their contribution was two-fold: first, they brought this form of treatment to the attention of members of the profession in this country; second, they insisted on intrauterine application of the element, in contradistinction to the vaginal or cervical approach. Kelly and Burnam insisted that the primary action of radium placed within the uterus is on the uterus, and not on the ovaries as is the case with roentgen rays; in 2 of their cases the fibroid tumor disappeared without cessation of menstruation.

From 1914 on, the literature has been voluminous, as would be expected, concerning an adequate type of treatment.

In benign disease of the uterus, the indication for treatment by radium is hemorrhage, but the underlying cause of this symptom must be sought.[22] The precise etiology is obscure. According to the accumulated literature, the most common contributory conditions are hyperplasia or polyposis of the endometrium, or uterine fibroid tumors; more rarely, repeated pregnancies, chronic endometritis of low grade, hypertension, fibrosis of the uterine muscle, cervical polyps, ovarian cysts, or blood dyscrasias such as purpura. When no physical basis for the symptom is ascertainable,

* Read at the Seventeenth Annual Meeting, American Radium Society, New Orleans, La., May 9–10, 1932.

TABLE I
INCIDENCE OF TYPES BY AGE*

Age by half decades	Cases	Per cent	Type of uterus																	
			Fibrous		Fibroid								Fibromatous							
			Normal size		Small		Moderate		Large				Small		Moderate		Large			
			Cases	Per cent	Cases	Per cent	Cases	Per cent	Cases	Per cent	Total cases	Total per cent	Cases	Per cent	Cases	Per cent	Cases	Per cent	Total cases	Total per cent
15–19	2	0.05	2	1.27																
20–24	2	0.05	2	1.27							2	1.61	3	4.61					3	2.18
25–29	11	2.63	6	3.82	2	5.00					4	3.22	1	1.53	2	3.38	1	7.69	4	2.91
30–34	25	5.98	17	10.82			4	5.00			22	17.74	7	10.76	7	11.86	1	7.69	15	10.94
35–39	70	16.75	33	21.01	10	25.00	12	15.00			31	25.00	25	38.46	19	32.20	5	38.46	49	35.76
40–44	122	29.19	42	26.75	12	30.00	17	21.25	2	50.00	41	33.06	17	26.15	20	33.89	3	23.07	40	29.19
45–49	107	25.60	26	16.56	8	20.00	32	40.00	1	25.00	41	33.06	10	15.38	11	18.64	3	23.07	24	17.51
50–54	65	15.55	22	14.01	4	10.00	14	17.50	1	25.00	19	15.32	2	3.07					2	1.45
55–59	11	2.63	4	2.54	4	10.00	1	1.25			5	4.03								
60–64	1	0.03	1	0.63																
65–69	2	0.05	2	1.27																
Total	418		157	37.55	40	32.25	80	64.51	4	3.22	124	29.66	65	47.44	59	43.06	13	9.48	137	32.77

* Average age, years.....43.85±0.235
Youngest, years.....15, fibrous type
Oldest, years.....67, fibrous type

endocrine imbalance is usually regarded as the causative factor. In planning treatment, the age of the patient, the presence or absence of fibromas and their size if present, the major complaints of the patient, and other conditions and complications associated with menorrhagia are of importance.

The present study consists of an analysis of all cases of benign uterine hemorrhage referred to the Section on Therapeutic Radiology of The Mayo Clinic for radium therapy during 1926 and 1927. There were 418 patients in all (Table I), of an average age of 43.85 years, varying from fifteen to sixty-seven years. Two hundred and twenty-nine patients (54.79 per cent) were in the fifth decade of life. Other statistics are given in Table I, and do not require comment, but part of the terminology used requires explanation. We have used the term "fibrous type of uterus" to designate a uterus which does not contain tumors, is of normal size, and which might be designated as normal were it not for the fact that it is the site of abnormal bleeding. We have also used the term "fibroid type of uterus" to designate a uterus that is definitely and diffusely enlarged but which does not contain any palpable fibroid tumors. Subdivisions of this class are as follows: a "small fibroid type of uterus" does not exceed in size that of a uterus in pregnancy of two months' duration; a "moderate sized fibroid type" of uterus corresponds in size to a uterus in pregnancy of from two to four and a half months' duration; a "large fibroid type" of uterus exceeds in size that of a uterus in pregnancy of more than four and a half months' duration. This enlargement in the large fibroid type may be due to fibroids, however not made out by palpation. The "fibromatous type of uterus" definitely contains fibromas (or fibromyomas), and is subdivided into subclasses, small, moderate, and large, on the same basis as that used in subdividing the fibroid type. As one would expect, the women with definite fibromas comprised a somewhat older group than those possessing a uterus of normal size; in the former only 16.03 per cent were less than forty years of age, compared to 38.19 per cent of the latter group.

Turning now to the major uterine complaints of these patients (Table II), it is seen that 285 (68.18 per cent) complained of menorrhagia and if metrorrhagia alone or associated with menorrhagia is added, the total increases to 408 patients, 97.59 per cent of our 418 patients. This leaves only a scattered 10 patients who complained of the other conditions named in the table.

Associated conditions, in many instances

TABLE II

INCIDENCE OF TYPES, ARRANGED ACCORDING TO MAJOR UTERINE COMPLAINT

Major uterine complaint	Cases	Per cent	Type of uterus					
			Fibrous		Fibroid		Fibromatous	
			Cases	Per cent	Cases	Per cent	Cases	Per cent
Menorrhagia	285	68.18	114	40.00	85	29.82	86	30.17
Metrorrhagia	30	7.17	13	43.33	8	26.66	9	30.00
Menorrhagia and metrorrhagia	93	22.24	27	29.03	29	31.18	37	39.78
Dysmenorrhea	5	1.19	1	20.00	2	40.00	2	40.00
Fibromas	3	0.71	1	33.33			2	66.66
Therapeutic menopause	1	0.23					1	100.00
Leucorrhea	1	0.23	1	100.00				
Total	418		157		124		137	

TABLE III

INCIDENCE OF TYPES, ARRANGED ACCORDING TO ASSOCIATED CONDITIONS*

Associated condition	Cases	Per cent	Type of uterus					
			Fibrous		Fibroid		Fibromatous	
			Cases	Per cent	Cases	Per cent	Cases	Per cent
Hypertension	30	8.15	15	50.00	9	30.00	6	20.00
Cardiac	21	5.70	7	33.33	9	42.85	5	23.80
Renal	2	0.54	2	100.00				
Diabetes	3	0.81			2	66.66	1	33.33
Secondary anemia	218	59.23	88	40.36	67	30.73	63	28.89
Arthritis	15	4.07	5	33.33	7	46.66	3	20.00
Hemorrhagic purpura	3	0.81	1	33.33	1	33.33	1	33.33
Syphilis	6	1.63			2	33.33	4	66.66
Hemophilia	1	0.27	1	100.00				
Cholecystitis	21		10		2		9	
Appendicitis	3				1		2	
Carcinoma of breast	8		4		2		2	
Duodenal ulcer	6		2				4	
Adenomatous goiter	18		4		7		7	
Exophthalmic goiter	1				1			
Myxedema	2		1				1	
Carcinoma of bronchus	1						1	
Hypotension	1				1			
Grand mal	1				1			
Jaundice	1		1					
Benign breast	3				1		2	
Poliomyelitis	2						2	
Multiple sclerosis	1				1			
Total	368	88.03						

* Fifty cases (11.96 per cent) had no associated major complication.

complicating the picture, were present in a large number of cases in our series (Table III). Certain facts revealed by this table are especially noteworthy. Only 50 patients (11.96 per cent) presented no major complication. The proportion of patients with marked secondary anemia was greater by 10 per cent among those whose uterus was fibrous than among those whose uterus was of fibroid or fibromatous type. Hypertension formed the second largest group of complications. Hemorrhagic purpura was diagnosed in 3 cases, and hemophilia in one. As shown by this large incidence of complications and associated findings, thorough general examination of these patients, as well as careful investigation of the pelvis, is essential. Moreover, especially if patients are more than forty years of age, diagnostic curettement is necessary. In our group of 418 cases, curettement, with or without other minor surgical operation, was carried out in 264 cases, 63.16 per cent of the entire group (Table IV). Including the curettements, some type of pelvic operation was performed at The Mayo Clinic or elsewhere within six months preceding the treatment with radium in all but 130 cases, 31.10 per cent of the total group.

In the control of uterine hemorrhage, in cases in which general examination has eliminated endocrine disturbance or blood dyscrasia as an etiologic factor, and in which curettage and microscopic study of the endometrial tissue so obtained have indicated that the disorder is benign, radium is the treatment of choice if certain contraindications listed below are respected. In some instances, however, treatment by roentgen rays or by extrauterine applica-

TABLE IV

INCIDENCE OF TYPES IN RELATION TO SURGICAL PROCEDURES PERFORMED WITHIN SIX MONTHS BEFORE TREATMENT BY RADIUM

Operations performed at The Mayo Clinic	Cases	Per cent	Type of uterus					
			Fibrous		Fibroid		Fibromatous	
			Cases	Per cent	Cases	Per cent	Cases	Per cent
Dilatation and curettage	213	78.88	76	35.68	74	34.74	63	29.57
Dilatation and curettage and removal of cervical polyp	13	4.81	3	23.07	3	23.07	7	53.84
Dilatation and curettage and cautery	20	7.40	10	50.00	5	25.00	5	25.00
Dilatation and curettage and puncture of cervical cyst	1	0.37	1	100.00				
Dilatation and curettage, cautery and excision of polyp	4	1.48	1	25.00	1	25.00	2	50.00
Dilatation and curettage and cautery puncture of cysts	2	0.74			2	100.00		
Dilatation and curettage, cautery, cautery puncture of cysts and removal of cervical polyp	1	0.37			1	100.00		
Dilatation and curettage and intraperitoneal shortening of round ligaments	1	0.37	1	100.00				
Dilatation and curettage and perineorrhaphy	5	1.85	2	40.00	1	20.00	2	40.00
Dilatation and curettage and amputation of cervix	1	0.37	1	100.00				
Dilatation and curettage and abdominal myomectomy	1	0.37					1	100.00
Dilatation and curettage and vaginal myomectomy	1	0.37					1	100.00
Dilatation and curettage, bilateral salpingo-oophorectomy and shortening of round ligaments	1	0.37					1	100.00
Removal of cervical polyp	1	0.37			1	100.00		
Vaginal myomectomy	2	0.74					2	100.00
Abdominal myomectomy, salpingectomy and oophorectomy	1	0.37					1	100.00
Total abdominal hysterectomy*	1	0.37					1	100.00
Pelvic exploration	1	0.37					1	100.00
Total	270	64.59	95	35.18	88	32.59	87	32.22
Operations performed elsewhere	18	4.30	7	38.88	7	38.88	4	22.22
No operation	130	31.10	55	42.30	29	22.30	46	35.38
Grand total	418							

* Treated for fibroid in broad ligament

tions of radium can be given. Such instances are those in which old chronic pelvic infection complicates the bleeding but in itself is not sufficient to require operation, and those in which large uterine fibroid is present, but there is definite contraindication to operation. Hysterectomy, hysterotomy or myomectomy is definitely indicated in a certain group of patients.

The contraindications to intrauterine application of radium in benign hemorrhage, the first of which has been referred to, are as follows: 1. Carcinoma of the uterine fun-

dus is mainly a surgical problem, and should be excluded by thorough curettage and pathologic examination before any treatment by radium is undertaken. 2. The uterine adnexa must be free from infection before intrauterine application of radium. Inflammatory disease of long standing, whether specific or not, may be activated by the manipulation necessary to application of radium, with subsequent peritonitis. However, application of vaginal radium packs, combined with surface radium packs, in our experience has proved a safe procedure. 3. Many authorities regard surgical operation as preferable for subperitoneal uterine fibromas, for these are not sufficiently influenced by intrauterine applications; surgical operation is preferred for submucous fibromas also, since they are more prone to infection and sloughing from treatment, and fibromas which cause enlargement of the uterus to a size greater than that in pregnancy of three to three and a half months' duration usually cause symptoms of pressure and are best removed at operation. Also, large fibromas, with calcareous degeneration are not affected by radium. 4. A rapidly growing fibroid tumor is best treated surgically; the rapid growth may be due to circulatory changes. 5. In cases of fibroma, with anemia out of proportion to the bleeding, operation is preferable, for the anemia may be due to degeneration of the tumor with absorption. 6. If pain is associated with a pelvic tumor, exploration is advisable, for the pain indicates additional pelvic lesions which should be investigated. 7. In cases of menorrhagia of girls and young women irradiation is a debatable procedure, but should be considered after failure to control the bleeding by medical measures. In cases of uterine fibroid in young women, myomectomy, or if necessary hysterectomy, with preservation of the ovaries, is preferable, for irradiation may cause artificial menopause with the usual distressing sequelae. 8. In any case of extrauterine pelvic tumor exploration should be made. 9. Radiophobia is sometimes cited as a contraindication; in the minds of some patients radium and roentgen rays are utilized only for carcinoma, and they recoil from any idea of irradiation.

Most of the cited contraindications for use of radium apply to cases of fibroid tumor. The percentage of fibroid tumors that is suitable for radium varies from the low figure of 30 per cent quoted by Miller to that of 70 or 90 per cent quoted by Ward;[6] probably two-thirds would be a better estimate, according to an editorial in the *American Journal of Roentgenology and Radium Therapy*. In cases of simple menorrhagia, if fibromas are absent, the paramount contraindications to intrauterine treatment with radium are adnexal inflammatory disease and youth of a patient. Even in the presence of adnexal disease, extrauterine irradiation may be cautiously used to advantage. For young patients, because at times even small doses of radium may produce permanent menopause, all other forms of treatment should first be attempted. Certainly in this younger group all simple, uncomplicated cases of menorrhagia that are not relieved by medical means are suitable for treatment by radium, and in cases of simple menorrhagia of the menopause, radium is, as Kelly phrases it, the modern medical miracle.

Regarding the technique of treatment, both radium and roentgen rays are used in this country, some preferring one agent and some the other. Treatment by roentgen rays has been outlined by Wood and other radiologists. In Europe roentgen rays are generally preferred. In treating fibroid tumors, especially growths of moderate or large size, a combination of the two may sometimes be of distinct advantage. In most cases curettement is indicated, and radium may be inserted as the final step of this operation. Regarding the dosage of radium employed, there is unanimity of opinion concerning the menopausal dose, which is gratifying when the wide variations of dose and method in the treatment of many forms of malignancy are considered. The dose generally employed is 1,200 mg-hr.;

the radium is placed in the uterine cavity and well screened to stop primary beta radiation. The following technique has been offered by Jarcho, who states that when the endometrium is at fault, as in glandular hyperplasia, endometrial polyps, simple hypertrophy or idopathic bleeding, 600 to 900 mg-hr. is sufficient. If the cause lies in the ovary or uterus, as in arteriosclerosis, chronic metritis, cystic degeneration of the ovary, loss of contractility of the myometrium, or premenopausal hemorrhage, 900 to 1,200 mg-hr. should be employed. Jarcho states that he used 1 mm. of platinum and 2 to 3 mm. of soft rubber as filters.

This brings up the question of the modus operandi of the treatment, whether radium placed in the uterine canal produces its effect on the endometrium or ovaries, or both. This question is not readily settled, for opportunity for pathologic examination of irradiated uterus and ovaries is rare. Clark and Norris stated that they had examined the uterus of numerous patients subjected to radium irradiation, and summarized their findings as follows:

"Radium produces a distinctly local macroscopic and histologic change that is similar in general character to the change produced by irradiation elsewhere, but is modified somewhat by local conditions. A localized sloughing or necrotic area is present, and this may, and generally does, involve the proximal layers of the myometrium, especially in those cases in which a moderately thorough curettage has preceded the irradiation. This area may be more than 5 cm. in length and 1 to 1.5 cm. in breadth but is generally considerably smaller. . . . The area of necrosis heals slowly, often persisting for weeks or even a few months. . . . Despite the lack of either macroscopic or histologic evidence of irradiation in the uterus some months after the treatment, the amenorrhea is generally permanent. The authors have examined many uteri in which, even after careful histologic examination, they were unable to demonstrate any evidence of previous irradiation. . . . Localized fibrosis of the myometrium at the site of the previous irradiation is observed at times, but these changes may be absent. . . . Whereas radium may cause obliteration of the blood vessels, such changes being observed in uteri in the immediate neighborhood of the irradiated site, these are generally quite localized and usually are not a prominent feature of the histologic picture."

The ovaries are reputed to be readily affected by irradiation; the follicles and corpus luteum are especially susceptible of destruction. Clark and Norris stated that they had examined a number of ovaries of patients treated by irradiation for benign hemorrhage (whether radium or roentgen rays were used was not specified), and reported that the follicles and corpus luteum were always absent, whereas in ovaries surgically removed after failure of irradiation, active follicles have nearly always been observed. Hence, Clark and Norris expressed the belief that the effect of intrauterine administration of radium is primarily on the ovaries, and only secondarily on the uterus. This conclusion was combated vigorously by Forsdike. He stated that the object of the treatment in menopausal hemorrhage is to convert the endometrium into connective tissue without production of necrosis, and that this is brought about by use of the hard gamma rays. The view prevalent in Germany, that the treatment is effective through castration, is erroneous, he said; the ovaries are practically unaffected; if one believes that the effect is on the ovaries, one ignores the inverse square law of dosage. In woman, he continued, the normal ovary is $3\frac{1}{2}$ inches away from radium placed in the fundus of the uterus, and demonstrable effect of radium on tissues extends only $\frac{3}{4}$ inch. Forsdike[9] presented clinical, pathologic and experimental evidence that the effect of radium is on the endometrium and not on the ovaries. Clinically, among his patients, aged twenty-nine to thirty-eight years, only 2 of 10 experienced flushes after treatment with radium; if the ovaries had been affected, the number would have been greater. In the age group thirty-nine to fifty years, menopausal symptoms were not unduly increased. As pathologic evidence, he examined the uterus of two patients after treatment by radium, and a section of

ovary from one of them. In sections of the uterus he found diminution in the number and size of the glands of the endometrium, and fewer capillaries than normal; there was no evidence of effect of irradiation in the section of ovary examined. In experimental work Forsdike used cats. The uterus of the cat is bicornate. A pregnant horn was opened, and the fetus removed; radium was implanted and the horn closed by suture. The ovary of the same side was attached to the uterine wall, and the opposite ovary was fixed at a distance of 8 cm. by suture and rubber tube (the same distance as the normal ovary of woman from the intrauterine applicator). The radium was removed after twenty-four hours. The experiment was repeated several times, and the animals were killed after twelve, twenty-one and sixty days. In all cases, the follicles of the ovary of the irradiated side were completely destroyed, whereas in the ovary fixed at a distance of 8 cm., there was no macroscopic or microscopic change. Hence, Forsdike concluded that in woman the ovary at a distance of 8 cm. is beyond the effective range of the rays from radium placed within the uterus.

To return to technique, Kelly and Burnam, who first in this country stressed intrauterine application of radium instead of intracervical or vaginal placement for the condition under consideration, have stated that they used radon in 1.5 mm. brass capsules enclosed in a brass applicator (wall, 2.5 cm. thick) attached to a uterine sound; the applicator was coated with sterile beeswax to reduce secondary radiation from the metal; under nitrous oxide anesthesia, curettage is performed, and 1,500 mc. of radon is introduced and left in place for one hour. At The Mayo Clinic, in the event of curettement, the radium is introduced at the time of the curettement, or within a few days, while the cervix is still open; 50 mc. of radon in 0.5 mm. of silver and 1.0 mm. of brass, covered with 2.0 mm. of soft rubber, is applied for twenty-four hours, to secure a full menopausal effect. This technique is generally in use, with minor differences in filtration. With patients who are below the age of menopause, however, important questions of dosage occur. Dosage varies according to the age.

From puberty to about the age of thirty years may be called the age of trial and repetition, as far as radium is concerned; radium is used for patients of this age group more as a therapeutic test, and its use can be safely repeated after a few months if the desired effect has not been attained. At this age, of course, more than the usual dose of 1,200 or 1,500 mc-hr. would ordinarily be necessary to stop menstruation permanently, but to preserve the reproductive powers and avoid the menopause we usually give a small dose; 200 to 300 mc-hr. is the usual amount chosen, and this may be repeated in a few months if necessary. In our series of 418 cases, a small intrauterine dose was employed in treating 16 patients, 2 of whom were aged more than thirty years, and the dosage averaged 212.6 mc-hr. In this age group radium should be considered only when all other medical and minor surgical means have failed; such measures as administration of glandular extracts and calcium lactate, dilatation and curettement, shortening of the ligaments, hysterectomy, myomectomy, removal of polyps, or puncturing of ovarian cysts. Often hyperplasia of the endometrium, or ovarian cysts, are found in these cases. The small dose of radium should not be exceeded, to avoid any possible injury to the ovary. Trial of radium is permissible if other measures have failed, and repetition of the small dose may safely be carried out two or three times, preferably at intervals of six months or more, if the first treatment does not regulate the periods successfully. If radium fails, hysterectomy, without removal of the ovaries, would be a last resort.

The next age group, thirty to forty years, is that in which caution must be used in respect to treatment with radium. A moderate dose should be employed, around 400 to 600 mc-hr. In our series of 418 patients, 68 received a moderate intrauterine treatment, the dosage averaging 476.26 mc-hr.

Kelly[15] warned never to exceed 700 mg-hr. if the wish is to preserve menstrual function. With hypofunctioning ovaries, even a moderate dose occasionally will produce permanent amenorrhea, but the average result of treatment, as with the small dose in the youngest group, is temporary cessation of menstruation, and return of normal flow after a few months.

The third age group, patients of more than forty years of age, is the ideal group from the standpoint of treatment. Preservation of the menstrual and reproductive function is not essential, and the full menopausal dose can be safely given, with almost uniformly good results. As mentioned before, the full menopausal dose, given within the uterus is around 1,200 mc-hr. In our series this dose was employed in 304 cases, and with radium surface packs in addition in 19 others; the average intrauterine dose was 1,113.42 mc-hr.

Results of radium therapy in cases of benign uterine bleeding are satisfying, especially in menopausal bleeding. We shall merely quote a few results reported from some of the larger clinics.

Neill,[17] from the Howard A. Kelly Hospital, reported results in treatment of 144 patients who were traced, of 176 patients in the age group forty to sixty-seven years. All the cases were examples of menopausal hemorrhage, without a demonstrable lesion, and cases of polyp, myoma, inflammatory conditions, and malignant disease were carefully excluded. In 85 cases bleeding ceased at once, and there was no subsequent menstruation; in the remaining 54 cases, 38 patients had one succeeding menstrual period, and 11 had two to four; of 5 patients treated by external irradiation, one menstruated four times, one twice, 2 once, and another had a radical operation elsewhere within a month. Two patients required further irradiation. Sixty-two of the total number had moderate hot and cold flushes and nervousness for periods of two months to three years; in 3 cases, these symptoms continued for more than five years. Pyometra developed in 3 cases, and was relieved by dilating the cervix; in another case, an acute pelvic inflammatory process supervened, and radical extirpation was performed within two months. There were no deaths. Kelly stated that slight abdominal discomfort may follow treatment for a month or more, and leucorrheal discharge for eight or ten weeks.

Kelly[13] reported 30 cases in which the patients were aged thirteen to twenty-five years; the dosage varied between 184 and 925 mc-hr., averaging 583 mc-hr. except in one case. In the exceptional case the patient was given 1,300 mc-hr. and underwent curettement four times; in her case the value for hemoglobin was 30 per cent. Regarding results in the 30 cases, in 16 the periods became normal immediately, or soon after treatment, and remained so. In 5, temporary amenorrhea occurred, with later return of normal menstruation after intervals varying between three months and four years. In 6 cases, permanent amenorrhea occurred, although in 4 the treatment had been given too recently to be sure that the result would be permanent.

Clark and Keene reported results in 527 cases of benign uterine hemorrhage due to myoma or myopathic hemorrhage; 476 patients were traced and 96 per cent were found to be cured. Six patients (1.2 per cent) needed a second treatment, and 18 patients (3.7 per cent) required subsequent operation. One patient died of peritonitis, a mortality of 0.18 per cent. The authors asserted that in surgical treatment of myomas the mortality rate varies from 2 to 7 per cent.

Norsworthy reported 121 cases; 13 patients were adolescents, and all were cured by intrauterine application of radium, averaging 150 mc-hr. Fifty-six patients had fibroid tumors; 51 were cured by intrauterine application of radium, and 5 underwent abdominal operation later. Five patients had associated adnexal disease; 3 were cured and 2 improved by use of radium. Forty-eight patients were at the menopausal age; 45 were cured, and 3 underwent abdominal surgery later.

Polak reported the results of treatment by radium in 96 cases of menopausal bleeding; 94 of the patients were traced. In 87 cases the uterus was atrophied, and there was no discharge as a result of treatment; in 7 cases the bleeding recurred and the uterus was removed. Polak also mentioned results in the treatment of myopathic hemorrhage of young girls. He used 200 to 300 mg-hr., with filtration of glass, silver, brass and rubber to remove the alpha

and beta rays. Thirty-one patients were treated, with an average dose of 250 mg-hr. In all except one case the result was successful. This patient required a second treatment. In all the cases the quantity of flow, as well as the duration, was regulated. Six of the patients were married and became pregnant; 3 had healthy living children.

In Germany, roentgen rays are used more than radium. In Döderlein's[12] clinic at Munich, 804 patients had been treated by irradiation from 1914 to 1927, mostly by roentgen rays. Since 1919, 408 patients were treated, and the bleeding of all but 13 was stopped successfully.

Forsdike,[10] in the *British Medical Journal*, reported treating 200 patients with excellent results. Fenwick, in the same journal, reported treating 89 patients, whose average age was forty-seven years. Of the 89 patients, 2 were not traced, one was not benefited, 13 were too recently treated to include in the report, and the remaining 73 were well. The one failure was in a case of a large submucous fibroid tumor. Fenwick further mailed questionnaires concerning menopausal symptoms to all his patients, and from the data so obtained stated that he could find no evidence that the climacteric induced by radium differed in any way, except in rapidity, from the normal period of disturbance experienced by women of middle age.

At The Mayo Clinic, Stacy and Mussey, in 1929, reported results in 244 cases of menorrhagia of the menopause in which the patients were traced. A second treatment with radium was required in 2 cases in which a moderate dose had been administered. Later, hysterectomy was performed in 3 cases; 2 of the patients had received a menopausal dose, and one a moderate dose. In 8 cases, menstruation remained irregular and profuse; in only one of these had a full dose been given. The result was excellent in the remaining 231 cases. In another group of 15 cases in which the ages were fourteen to twenty-one years, however, the results were varied. The dosage varied between 100 and 700 mg-hr. One patient was given 150 mg-hr. without improvement, and another, with the same dosage, ceased menstruating for three years. Of 4 cases in which normal menstruation was obtained 150 mg-hr. had been given in two, 300 mg-hr. in one, and 200 mg-hr. in one. In the entire group of adolescents all practicable medical and surgical measures had first been tried without success.

Ford presented a comparative study of irradiation and surgical treatment for fibromyoma from The Mayo Clinic; 245 patients were treated by radium, and 250 by surgery. There was one death among those treated with radium, a mortality rate of 0.29 per cent, and 2 deaths among those treated surgically, a mortality rate of 0.8 per cent. Otherwise, the advantage appears to lie with surgery in the treatment of fibromyoma, for only 4 per cent o failures occurred in the surgical group, whereas 18 per cent of the patients treated by radium required further irradiation, and subsequent operation was necessary in 13.7 per cent.

That a relatively unsatisfactory showing in the results of treatment by radium may be due to injudicious selection of cases and to excessive caution in dosage is indicated by the results reported from the Howard A. Kelly Hospital by Neill.[18] He treated 741 patients with fibroid tumors by means of radium, and the outcome was successful, except that 43 patients (5.8 per cent) were given a second treatment by radium, and 33 (4.4 per cent) required hysterectomy elsewhere within a year. There were no deaths.

Regarding the 418 patients treated at The Mayo Clinic in 1926 and 1927, and which form the basis of the present study, positive results can be given in only 295 cases (70 per cent), at this time (Tables v and vi). At a later date a more complete report will be given. We have graded the results as "good," "fair," "indeterminate," and "failure" (Table v). The purpose of the treatment, by which the amount of treatment was governed, determined the result; for example: complete amenorrhea, effected by a small dose given to an adolescent, would not be a good result, whereas complete amenorrhea, produced by a menopausal dose given to a patient at the age of menopause would be a good result. Hence, the results in the cases in which the patients were traced are figured according to the dosage employed; the small dose (averaging 212.6 mc-hr.), the moderate dose (averaging 476.26 mc-hr.), and the menopausal dose (averaging 1,113.42 mc-hr.). With a small dose, a good result was considered to be reëstablishment of normal menstruation for a period of at least a year; a fair

TABLE V

INCIDENCE OF TYPES WITH RELATION TO DOSAGE OF RADIUM AND RESULT

Age group, years	Dose	Type of uterus and result of treatment																	
		Fibrous						Fibroid						Fibromatous					
		Good	Fair	Indeterminate	Failure	Patients not heard from	Total	Good	Fair	Indeterminate	Failure	Patients not heard from	Total	Good	Fair	Indeterminate	Failure	Patients not heard from	Total
15–24	Small	3					3												
25–34		2	1		1	1	5		1			2	3		1		1	1	3
35–44														1					1
45–54												1	1						
55–64																			
65–74																			
Total		5	1		1	1	8		1			3	4	1	1		1	1	4
Per cent		71.42	14.28		14.28	12.5			100.0					33.33	33.33		33.33	25.00	
15–24	Moderate					1	1												
25–34		7	4		2	5	18	2					2				1		1
35–44		13	3	1		6	23	3	4	1		5	13	6				1	7
45–54		2					2												
55–64		1					1												
65–74																			
Total		23	7	1	2	12	45	5	4	1		5	15	6			1	1	8
Per cent		69.69	21.21	3.03	6.06	26.66		50.00	40.00	10.00		33.33		85.71			14.28	12.5	
15–24	Menopaus. l																		
25–34												1	1	2	1				3
35–44		34	4			14	52	19	8			13	40	33	7		1	15	56
45–54		32		2		12	46	35	2	1		21	59	45	1			18	64
55–64			1			3	4	3				2	5		1			1	2
65–74		1		1			2												
Total		67	5	3		29	104	57	10	1		37	105	80	10		1	34	125
Per cent		89.33	6.66	4.00		27.88		83.82	14.7	1.47		35.23		87.91	10.98		1.09	27.2	
Grand total		95	13	4	3	42	157	62	15	2		45	124	87	11		3	36	137
Total per cent		82.6	11.3	3.47	2.6	26.75		78.48	18.98	2.53		36.29		66.41	8.39		2.29	26.27	

TABLE VI

INCIDENCE OF TYPES WITH RELATION TO OPERATIONS WHICH WERE PERFORMED WITHIN TWO MONTHS AFTER APPLICATION OF RADIUM

Operations at The Mayo Clinic	Cases	Per cent	Type of uterus					
			Fibrous		Fibroid		Fibromatous	
			Cases	Per cent	Cases	Per cent	Cases	Per cent
Vaginal hysterectomy	1	4.54					1	100.00
Subtotal abdominal hysterectomy	2	9.09			1	50.00	1	50.00
Subtotal abdominal hysterectomy and salpingo-oophorectomy	5	22.72			3	60.00	2	40.00
Total abdominal hysterectomy and salpingo-oophorectomy	4	18.18	1	25.00	1	25.00	2	50.00
Watkins-Wertheim interposition operation and perineorrhaphy	2	9.09	1	50.00		50.00		
Dilatation and curettage	8	36.36	4	50.00	4	50.00		
Total	22	5.26	6	27.27	10	45.45	6	27.27
Operation elsewhere	5	1.19	2	40.00	1	20.00	2	40.00
No operation	391	93.54	149	38.10	113	28.90	129	32.99
Grand total	418							

result was good control of menstruation for at least six months; an indeterminate result would be that the patient reported that she was not certain regarding the favorable influence of the treatment, and failure was inability to produce a favorable change in the bleeding for a period of six months after treatment. Similarly, with a moderate dose, we considered establishment of normal menstruation to be our object, or complete amenorrhea if a patient was at the age of menopause; fair control of menses for at least a year constituted a fair result; if a major surgical procedure was necessary for menorrhagia within two months of the treatment, we called the result indeterminate, and finally no control of bleeding by our treatment, following an interval of four to six months, was rated a failure. With the menopausal dose, complete amenorrhea, or temporary amenorrhea, with succeeding normal menstruation, constituted a good result; a fair result was recorded when control of bleeding was merely "fair," or when normal menstruation occurred after six months or a year of amenorrhea; if major operation (Table VI) was performed for the menorrhagia within two months of the treatment we charted the result as indeterminate; if flowing continued, and hysterectomy or irradiation was necessary subsequently (later than two months), we recorded a failure. On reviewing our 295 cases in which the patients were traced, we found only 6 failures (2.02 per cent).

COMMENT

The 418 patients treated with radium at The Mayo Clinic for benign uterine hemorrhage constituted a carefully selected group. All received treatment with radium. Only 15 patients (3.59 per cent) were less than thirty years of age, and in this small division all feasible medical and minor surgical measures had first been attempted without success. Some surgical measures (in most cases curettement) preceded the treatment in all but 130 of the total number of cases. Patients whose uterus was larger than that produced by a pregnancy of four and a half months' duration or which contained fibroid tumors forming a

pelvic mass of this size were not accepted as a rule for treatment with radium; in this series only 17 patients (4 per cent) were in this category.

The small dose, applied to 11 traced patients, was given entirely to young persons, except in one instance. Patients less than forty years of age formed another group, which was perplexing as far as dosage was concerned, and whether to give a moderate or a menopausal dose was often decided by the patient's own inclination in the matter. The possible untoward effects were always fully explained to the patient, and her cooperation, as far as possible, was always secured before deciding on any plan of treatment. The therapeutic menopausal dose was usually recommended for the older age groups.

CONCLUSIONS

For benign hemorrhage of the menopause not related to uterine fibromyoma, intrauterine treatment with radium is practically a specific. The major contraindication is the history of or the presence of adnexal inflammatory disease, and with this complication both vaginal and external treatment with radium has proved a safe procedure in a limited number of cases. Among patients of the younger age groups, bleeding can be controlled and the condition cured by intrauterine application of radium in the majority of cases; however, in a small percentage of cases premature menopause will occur in the presence of hypo-ovarian function that is not recognizable beforehand. Hence, the possibility of permanent amenorrhea and loss of reproductive power must be explained to the patient before treatment, and it is wise to employ all possible medical and minor surgical measures first. If radium is employed, a small dose should be attempted, with repetition in a few months if the desired effect is not attained. If radium fails final recourse must be to surgery.

In the treatment of fibroid tumors causing menorrhagia, probably selection of cases is too conservative. Intrauterine treatment with radium, in conjunction with external application of radium or roentgen rays, affords good results even with large fibromas, and is worthy of consideration if the pelvis is otherwise normal and the surgical risk excessive. If the diagnosis is at all questionable, operation is preferable. There is also a large group of patients with fibromas whose hemoglobin is of low concentration and whose resistance is so diminished that they constitute poor surgical risks; treatment with radium and roentgen rays, if not curative in themselves, will build these patients up so that they are more suitable for subsequent operation. Therefore in the control of menorrhagia one has three agents at hand and the results obtained depend on the careful selection of the method of treatment in the individual case.*

* For discussion see page 520.

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THE FATE OF FIBROMYOMA OF THE UTERUS AFTER RADIOTHERAPY*

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IT IS the conventional teaching in most gynecological clinics that fibromyomata which have reached a size greater than that of a three months' pregnancy should be removed because of doubt of the efficacy of this form of treatment in reducing the size and relieving the symptoms of these tumors; because of the danger of coexisting adnexal lesions and of subsequent changes (sarcoma and degeneration) in the growth; because of a belief that fibromyoma predisposes to adenocarcinoma of the body of the uterus, and lastly, because of the increased possibility of diagnostic error with masses of the larger size. In a study of the literature many reports of remarkable cures and dismal failures were found, but there is lacking a comprehensive review of such cases based on a prolonged follow-up observation. It has been our good fortune to have available an efficient follow-up system. We have therefore been able to follow a group of women with large myomata, treated by radiotherapy, over an average period of seven years (one to eighteen years), and by personal examination to determine correctly the fate of the tumors and the occurrence of the complications above mentioned.

Among 452 women treated by roentgen rays and radium for uterine bleeding and fibromyoma, there have been 130 who had a uterus larger than that of a three months' gestation of whom 112 have been examined. They were treated for the most part by diagnostic curettage followed by an intrauterine application of radium in doses of from 600 to 4,800 mg-hr., filtered by 0.5 mm. of silver to 1.0 mm. of platinum. Some of these have subsequently been treated by roentgen radiation. The earlier cases were treated by roentgen rays alone. Hemorrhage was the indication for treatment in all but a few who suffered from pain, urinary distress, or the mechanical presence of the tumor.

This study will not consider the results of the treatment on symptoms but only those anatomical effects, good and bad, which have a bearing on the treatment, especially to discover if by this method, which removes no organs, harmful conditions are allowed to remain.

Considering the problems arising at or immediately after the treatment, we find that one woman died of embolism eleven hours after diagnostic curettage and the insertion of radium. There was one serious diagnostic error. A woman with a rapidly growing uterine tumor was scheduled for hysterectomy, developed a cold, but against our judgment, insisted on being treated. She was given a sterilizing dose of radium, was amenorrheic for six months, again began to bleed, was operated upon and found to have a sarcoma. Death followed eighteen months after the original operation. Of cases showing degeneration in the fibroid following radiotherapy, there is only one possibly of importance. A woman thirty-five years of age with a uterus the size of a five months' pregnancy, after diagnostic curettage, was given a sterilizing dose of roentgen radiation. She had a normal period one month later. A week after this she was seized by moderate right-sided pain, maximum over an area in the tumor 5 to 6 cm. in diameter where there was also tenderness. There was a temperature of 101°F., slight prostration, and slight leucocytosis. The symptoms rapidly subsided. At the end of a year the uterus was the size of a two months' pregnancy. Whether this was an irregular menstrual congestion such as is often seen after a normal or artificial menopause or

* Read at the Seventeenth Annual Meeting, American Radium Society, New Orleans, La., May 9–10, 1932.

whether there was a true degeneration is not known.

Five cases were operated upon because of the persistence or recurrence of symptoms.

(1) A woman of forty-three with severe metrorrhagia and a uterus the size of a four months' pregnancy received 1,200 mg-hr. of radium and later one-half a sterilizing dose of roentgen rays. She continued to have periods, moderate at first but later profuse and had a hysterectomy a year after the first treatment. A case of insufficient dosage living in another town and not under control.

(2) A woman of thirty-six with menorrhagia and a uterus the size of a three months' pregnancy was treated by 1,200 mg-hr. of radium. She continued to bleed and had an hysterectomy six months after the original operation. Another case of insufficient dosage.

(3) A woman of forty-eight with urinary frequency and a uterus the size of a four months' pregnancy was treated by dilatation and curettage followed by a sterilizing dose of roentgen rays. The symptoms were unrelieved although at the end of a year the uterus was only the size of a two months' pregnancy. She was operated upon in another hospital. The results of operation are not known. This was an ill-advised application of the method. Probably the urinary symptoms were not due to the tumor. At any rate the effect upon urinary symptoms after the artificial menopause have been poor.

(4) A woman of forty with severe metrorrhagia, marked secondary anemia, thrombophlebitis of an internal saphenous vein and a mass the size of a seven months' pregnancy was kept two weeks in bed. The phlebitis improved but hysterectomy was thought hazardous. Bleeding continued to be severe. Therefore, dilatation and curettage was performed, with the application of 2,400 mg-hr. of radium followed by a sterilizing dose of roentgen rays. Amenorrhea followed. At the end of a year, the patient was in perfect health. The mass had reached the size of a five months' pregnancy, but because of a return of bleeding, hysterectomy was performed.

A case of fibromyoma which demanded hysterectomy but because of the poor operative risk was treated by radiotherapy with resulting return to health so that later operation was safely performed.

(5) A woman of fifty-one with menorrhagia and a uterus reaching well above the umbilicus. Because of a mild heart lesion, radiotherapy was advised. She was given 2,400 mg-hr. of radium, followed by a sterilizing dose of roentgen rays. Bleeding continued. She was given a second sterilizing dose of roentgen rays. The mass shrank to a level below the umbilicus. Hysterectomy was performed because of the bleeding.

A case of frank failure of the method to stop the bleeding.

Of the late complications of a serious nature occurring in the pelvis, there was one case of carcinoma of the body of the uterus appearing eight years after a sterilizing dose of radium for a tumor the size of a four months' pregnancy. One woman had a carcinoma of the cervix eight years after roentgen therapy for a tumor the size of a five months' pregnancy, and another a squamous cell epithelioma of the cervix

Table I

Reduction in size of tumor

Original Size	Satisfactory Reduction				Unsatisfactory Reduction			Followed	Not Followed	Total Cases
	50 per cent	75 per cent	Complete	Totals	None	Slight	Totals			
3–4 mo.	5	19	66	90 (94.7%)	3	2	5 (5.3%)	95	17	112
5–6 mo.	2	6	4	12 (92.3%)	0	1	1 (7.7%)	13	1	14
7–8 mo.	0	1	1	2 (50.0%)	0	2	2 (50%)	4	0	4
Total	7 (6.3%)	26 (23.2%)	71 (63.4%)	104 (92.9%)	3 (2.6%)	5 (4.5%)	8 (7.1%)	112	18	130

seven years after dilatation and curettage and a sterilizing dose of radium in a uterus the size of a four months' pregnancy. In all of these women the fibroid had almost completely disappeared. In 2 women there occurred a cystadenoma of the ovary, one after seven years and the other after four years. It is remarkable that aside from these tumors of the ovaries, there have been no cystic ovaries. There was no case of sarcoma of the uterus, disease of the tubes or carcinoma of the ovaries discovered.

The effect on the size of the tumor is expressed in Table 1. It shows that there has been no case in which the tumor increased in size, 3 cases where it was unchanged, and 5 in which the reduction was so slight that it was unsatisfactory. In 104 the reduction proceeded to a satisfactory degree during the period of observation; in 71 the uterus became of normal dimensions; in 26 the mass at the last observation was one-fourth of the original size and in 7, one-half the original size. Data on which to base a prognosis as to the probable decrease in size of the myoma were not informative except that a softer and apparently more recent growth seemed to shrink more satisfactorily than one of long standing and hard consistence. This may be because of the large amount of hyaline and calcareous tissue in the old, hard growths and the greater proportion of vascular myomatous tissue in those which are susceptible. Variation in the degree of shrinkage was striking. In one woman a tumor the size of a four months' pregnancy treated by an intrauterine application of 25 mg. of radium with a screen of 0.5 mm. silver for twenty-four hours had disappeared in four months. Another mass the size of a five months' pregnancy treated by 2,400 mg-hr. radium, followed by two series of roentgen treatments, each sufficient to sterilize the average woman, shrank only slightly during two years of observation. The duration of the process of shrinking may be very long, as in the case of a tumor originally the size of an eight months' pregnancy, which after three years was the size of a four months' pregnancy and after five years that of a six weeks' pregnancy, and after fifteen years smaller than the average uterus. So in planning an ideal procedure, one is at a loss to estimate the correct maximum dosage. A wise and, with few exceptions, effective technique is to introduce into a uterus of three to four months' size, 1,800 to 2,400 mg-hr. of radium with 0.5 mm. platinum screen, to be followed after two months, if amenorrhea does not ensue, by an erythema dose of short wave, highly filtered roentgen rays over the lower abdomen and sacrum. For larger tumors, this dose is increased, the effectiveness being determined by the presence of a permanent amenorrhea.

The details of technique are often not given in articles dealing with the application of radium for the treatment of uterine bleeding and myomata. Also from personal contacts it would appear that the introduction of radium in the hands of many gynecologists is a routine affair: the installation of the same applicator in much the same fashion for all cases. It must be remembered that the dose will vary according to (1) the amount of radium, (2) the distribution of the radium, (3) the time, (4) the distance of the radium from the tissues to be attacked and (5) the screening. A common source of error is indicated in Figure 1 where the displacement of an ovary brings into play the law of inverse squares.

The mechanism of reduction is a matter of considerable speculation but little proof. The sclerosed hyaline fibroids found after radiotherapy and after the menopause have much the same appearance. I believe that the shrinkage is due mostly to the effects of the menopause and less to direct effect on smooth muscle and the blood vessels. In only one tumor was there progressive shrinkage while menstruation persisted. Until, therefore, amenorrhea is permanent, it is unsafe to consider the mass controlled, and if—although I have not had the experience—a pelvic tumor should increase in size after a permanent amenorrhea had

been established, I should doubt the diagnosis and perform an exploratory laparotomy.

A study of these results would indicate that where the mass is of moderate dimensions, there is very little likelihood that it will harm the patient after she has received a full sterilizing dose of roentgen rays or radium. Where the indication for treatment is uterine hemorrhage, the presence of a mass the size of a three to four months' pregnancy need not militate against the induction of an artificial menopause. Such a mass with a sterilizing dose of roentgen rays and radium will with reasonable certainty shrink to unimportant proportions. With tumors larger than a six months' pregnancy, our experience would indicate that in the long run radiotherapy is less satisfactory than removal even though bleeding may be controlled. The constant supervision, the attitude of mind of a woman who knows that she has a large tumor, frequent follow-up examinations, the necessity for intensive and probably repeated roentgen treatments, the possible danger of degeneration or toxemia from absorption, the greater difficulty in diagnosis, and the less satisfactory results, make radiotherapy inferior to operation in those women who are excellent surgical risks. It is important, however, that we should be strict in our criteria for the determination of operability. The results here reported are excellent enough to demand that the mortality from operation be reduced to that represented by accidents such as embolism, pneumonia, and intestinal obstruction. There should be no deaths from shock, hemorrhage, or cardiac failure. This restriction may even be applied after the abdomen is opened. A partial success with radiotherapy given after the incompleted operation is better than the loss of the patient.

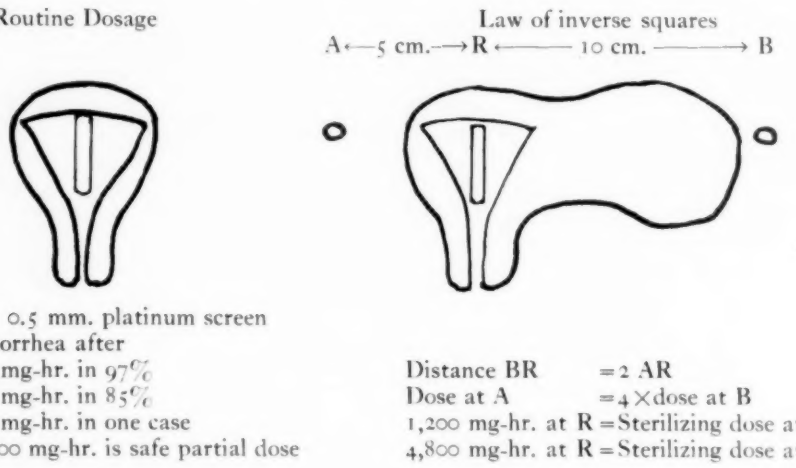
Routine Dosage
Law of inverse squares
A ← 5 cm. → R ← 10 cm. → B
0.5 mm. platinum screen
Amenorrhea after
1,800 mg-hr. in 97%
1,200 mg-hr. in 85%
600 mg-hr. in one case
300–400 mg-hr. is safe partial dose
Distance BR =2 AR
Dose at A =4 × dose at B
1,200 mg-hr. at R = Sterilizing dose at A
4,800 mg-hr. at R = Sterilizing dose at B

Fig. 1. Radium technique—the artificial menopause. Illustrating a common source of error in the treatment of fibromyoma of the uterus.

SUMMARY

There have been presented observations made from two to eighteen years after treatment on 112 cases out of 130 who have received radiotherapy in the treatment of fibromyomata of the uterus of a size larger than that of a three months' pregnancy. They show that there was one serious diagnostic error (sarcoma); there was one death from embolism eleven hours after dilatation and curettage. In one case there was some evidence of degeneration in a uterus the size of a six months' pregnancy but with complete recovery and shrinkage of the mass. Five cases required subsequent operation; three because of the re-

currence of the bleeding, one because of failure to relieve urinary frequency and one because of persistence of bleeding and only slight reduction of the mass. Of the late complications, there was one case of carcinoma of the body of the uterus, one of squamous cell epithelioma of the cervix, and two cystadenomas of the ovary. There occurred no cystic ovaries and no sarcoma of the uterus. The shrinkage of the tumor mass was complete in 63.4 per cent of the cases; to one-quarter of the original size in 23.2 per cent and to half the size in 6.3 per cent. There was no reduction of the size of the mass in 2.6 per cent and a slight but unsatisfactory reduction in 4.5 per cent.

CONCLUSIONS

1. In treating myomata larger than the size of a three months' pregnancy, the question of diagnosis is the most serious and most difficult and far outweighs the question of the mode of treatment.

2. There were no serious tumor changes (sarcoma, degeneration) in 112 cases followed for an average period of seven years.

3. Following radiotherapy in a sterilizing dose, there can be promised a satisfactory shrinkage in 90 per cent of the myomata so treated, the results being more satisfactory in the masses of moderate size.*

* For discussion see page 520.

TREATMENT OF BENIGN UTERINE NEOPLASMS, WITH SPECIAL REFERENCE TO THE USE OF RADIUM*

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SAN ANTONIO, TEXAS

IN benign uterine neoplasms the chief method of treatment may be considered under four divisions: (1) Let alone and observe; (2) operation; (3) roentgen rays; (4) radium. None of the methods is antagonistic to nor exclusive of the others, and cases for each method of treatment are fairly well defined. After a definite diagnosis one should have no difficulty in deciding the treatment in any given case. Each has a field; however, the edges overlap in some instances. The method of treating benign uterine neoplasms depends largely on the age of the patient, the patient's physical condition, the local symptoms present, the size of the tumor, and the past history of the patient with special reference to peritoneal infection. The method of treatment should control hemorrhage, remove the tumor, or check its growth, impair the function of the organ as little as possible, and with a minimum mortality risk.

A uterine neoplasm producing no symptoms, especially if indurated and nodular, should be classed under the "let alone and observe" treatment. The mere fact of the presence of tumor is not sufficient to warrant operation or irradiation. Operation meets all of the requirements, except the mortality risk, and its possibilities should be considered in all cases of benign uterine neoplasms causing symptoms in women under thirty-five years of age. While the mortality following myomectomy ranges from 0.5 to 1 per cent in clinics conducted by our most skilled surgeons, it is nil following the use of radium or roentgen rays. Roentgen irradiation affords a most satisfactory treatment in large tumors producing pressure symptoms. It will arrest hemorrhage and cause reduction of the tumor, enabling the use of operation or radium later for permanent relief.

Radium meets all the requirements except that of impairing the function of the organ, and its possibilities should be considered in all women over thirty-five years of age. Sufficient radium irradiation to produce permanent effect on a uterine neoplasm would in all probability destroy ovarian function. An accurate pretreatment diagnosis is of more importance when radium is considered than for roentgen-ray or operative treatment. Although all neoplasms will respond to radium irradiation so far as hemorrhage is concerned, a careful study from every viewpoint should be made before deciding the method of treatment.

Removal by operation is indicated in the majority of cases met with in general practice; also in cases diagnosed at the larger charity clinics, where mostly poor people of all nationalities come. In that class neoplasms, when present, are most often larger and associated with pressure or inflammatory symptoms. Neoplasms calling for removal by operation are: (1) those larger than a four months' pregnancy unless the physical condition of the patient is a contraindication; (2) calcified tumors; (3) pedunculated tumors; (4) tumors associated with symptoms of impaction; (5) tumors accompanied by inflammatory or adnexal disease; (6) tumors associated with acute or chronic pelvic infection; (7) some cases of definite neurasthenia (radiumphobia.)

Myomectomy and subtotal hysterectomy, the two operations of choice, should be accepted as serious operations. While myomectomy has a greater operative mortality, it should be favored in young girls and child-bearing women. Myomectomy and subtotal hysterectomy sometimes fail to relieve the chief symptoms for which the

* Read at the Seventeenth Annual Meeting, American Radium Society, New Orleans, La., May 9–10, 1932.

operation was performed, that of hemorrhage. In such conditions radium should be most welcome.

Several cases in our clinic that had had subtotal hysterectomy, in which bleeding continued for months, were relieved by the use of radium through the vagina. Three cases that had had complete or partial double ovariotomy, followed by continuous bleeding, were promptly relieved by intrauterine application of radium. While myomectomy does permit greater possibilities for pregnancy than radium rays, pregnancy and normal delivery of a normal child in cases of fibroids without treatment of any kind are not infrequent.

Radium applied within the uterus is indicated: (1) in small neoplasms accompanied by hemorrhage; (2) in selected cases of large neoplasms; (3) in operative cases when the patient is too ill for an abdominal operation. Radium will control hemorrhage, it will produce menopause, it will arrest growth of the neoplasm, reduce its size and in a large majority of cases cause complete disappearance of the neoplasm. In young girls, or child-bearing women, it may be used to check excessive menstruation temporarily, permitting the ovaries to rest followed by re-establishment of a normal flow. Care should be exercised in girls and young women that permanent menopause or injury to the ovaries is not brought about. While one should expect permanent menopause after menstruation has been suppressed for twelve months, cases have been reported in which menstruation returned and pregnancy followed two years afterwards. Such did not occur in our series. We guard against injury to the ovaries in all younger women and girls.

Hysterectomy should be considered only in cases in which myomectomy would be unsafe and in which radium is contraindicated, except in women who prefer removal of the uterus to the use of radium. Some women have "radiumphobia" caused by the newspaper reports of the New Jersey Watch Company's experience, strengthened by the advice of gynecologists and surgeons who have had no experience with the use of radium. No abdominal operation has reached a higher degree of technical perfection, nor has more satisfactory postoperative results, than hysterectomy as is usually performed for benign uterine neoplasms. For this reason, it is difficult to convince the gynecologists that any other method of dealing with these neoplasms can be compared with operation. Any method of treatment to be accepted must be proved to offer permanent relief and to be safer than operation. Radium will fulfill these requirements in selected cases.

Supravaginal hysterectomy, which is the operation most popular for benign uterine neoplasms, was first introduced by Charles Clay, of England, in 1834. Clay's first few cases died, and not until 1863 did he have a successful result. Following Clay's experiences many surgeons practiced hysterectomy with fatal results under mistaken diagnosis for that of ovarian tumors. Kimbell of Lowell, Massachusetts, did the first successful hysterectomy for fibroids under a correct diagnosis. Lawson Tait was the first to advocate the removal of the ovaries for fibroids of the uterus. Ovariotomy was the accepted treatment for fibroids of the uterus, until during the early eighties. This mistaken idea was due to the fact that the tumors decreased materially in size after the menopause. During the last twenty years radium has been used in the treatment of uterine neoplasms with increasing popularity and success. With perfection of technique and selection of cases, one is justified in placing radium as a safe, sure, and economical, treatment for uterine neoplasms of any type.

In adolescent girls and young women radium is a very dangerous agent. Maternal possibilities and sexual life are both of paramount importance. Radium, however, is of great value in arresting the growth of a tumor and to check hemorrhage, permitting the patient to rebuild for operation.

Sufficient radium irradiation to permanently check growth or to remove a tumor would probably destroy ovarian function,

and should be carefully guarded in child-bearing women. In the group of women over thirty-five, neither of these important functions is so much endangered. Again, 20 per cent of all women over thirty-five have benign tumors of the uterus, most of which are fibromyomas, and 30 per cent who are congenitally sterile, reduces the chance of sterilization of women over thirty-five years of age to a small possibility. In women past forty-five years of age radium is without question the treatment of choice unless contraindicated.

There is no more satisfactory classification of uterine neoplasms than the time-honored division, benign and malignant. Proof is positive, however, that both benign and malignant growths have definite histological characteristics, but there are intermediate stages which cannot be sharply defined in relation to any specific structure. Neoplasms varying in consistency from calcification to almost fluid may be found in the same pelvis and their response to different forms of treatment would depend largely on their consistency. For example, a calcified tumor may be found among multiple fibroids in the same case, while another type as soft as a ripe fig may be found, and still another as viscous as jelly. The soft viscous type would probably recur after removal by operation, but not after intrauterine application of radium. The soft fig-like tumor would disappear without fear of recurrence after complete removal by operation or the use of radium.

The calcified growth can be removed only by operation. Multiple types of such tumors are usually found in women under thirty-five years of age and are seldom diagnosed in their early stages; more are diagnosed after abdominal incision.

Uterine fibroids, so far as is known, are benign and many produce no symptoms. Others produce a multitude of complaints. Fibroids are more common after the age of thirty-five, but may be in either older or younger women. Fibroids tend to produce sterility. They are prone to prolong menstruation. They vary in size and rapidity of growth. Many fibroids cease to grow and in rare instances disappear after menopause. Large indurated growths seldom cause the excessive bleeding usually associated with the smaller and softer type. In the large neoplasms cystic or necrotic changes may take place. Hyaline changes with areas of calcification are not uncommon. Sarcomatous changes are exceedingly rare; in fact, sarcomatous changes have not been proved to occur. Reports are published in which fibroids of apparently simple structure have destroyed life. These reports, however, should be accepted with the knowledge that the uterus is occasionally the seat of true sarcomata, which in their early stages present symptoms clinically characteristic of fibromyomata. It is difficult to decide between the slow-growing, spindle cell sarcoma, fibrosarcoma, and the gelatinous fibroid, and one cannot argue from present knowledge that neoplasms do undergo transformation into sarcomata. Prior to laboratory studies but few neoplasms had a better reputation for innocence than dermoids. Now we have learned that the less typical type of dermoid is prone to disseminate. There is no positive evidence on record that innocent fibroids take on sarcomatous degeneration unless complicated with trauma or infection. Most gynecologists leave the cervix when operating for benignancy of the body of the uterus, and there are no definite convincing records of sarcomatous changes in the cervical stump, which gave no evidence of abnormality before operation. There can be no substantiated objection to the use of radium in such cases, even if such fears were well founded; sarcomata react well to radium rays.

About 4 per cent of suspected uterine fibromyomata are found to be malignant. Many of these are diagnosed following curettage, which should have been diagnosed from clinical history before reaching the operating table. The menstrual flow may be profuse and prolonged, but with well-defined menstrual periods in which there is no intermenstrual bleeding or foul dis-

charge, one is reasonably safe in diagnosing as non-malignant. On the other hand, intermenstrual spotting, which soon develops into continuous flow, with an increase at the regular period, accompanied by odor, should be suspicioned as malignant. In cases presenting anemia out of proportion to the small amount of blood, or decided toxemia, a degenerative tumor should be considered, which speaks against radium.

Large fibromyomata should be treated by myomectomy when possible in child-bearing women in the absence of contraindications, but in cases that have hemorrhage to a dangerous degree, radium will check the hemorrhage and permit the patient to rebuild for an operation with safety. It is unsafe to give sufficient radium to insure autolytic cell destruction; especially is this true in large irregularly shaped tumors, on account of possible necrosis and sepsis.

A small, subperitoneal fibroid may exist for years without increasing in size, or without giving rise to symptoms. Such tumors often remain unchanged until menopause, and then disappear entirely so far as gross examination goes, while others take on an unusually rapid growth after menopause. The presence of fibroids often delays menopause. If, however, it is associated with menorrhagia or metrorrhagia, or with pressure symptoms, treatment of some form should be instituted.

Submucous growths of the uterus, while quite responsive to radium, owing to their susceptibility to infection and sloughing after intrauterine trauma from any cause, should not be routinely treated with radium. However, if tumors are small, and do not obstruct the uterine canal, they may be removed entirely with radium without risk of infection. In cases that have bled to a low ebb, radium without question will check hemorrhage, and permit the patient to rebuild for operation. The one characteristic possessed by all fibroids is a well-developed capsule, a structure of vital importance to the life of the neoplasm, which should be removed with the tumor.

In case of doubt as to diagnosis or as to location of growth, with reference to the uterus, we dilate and curette for biopsy, and apply radium in tandem from the top of the fundus to the cervix at the time of curetting, and complete the treatment after laboratory report. In former years, we advised hysterectomy in all cases of malignancy of the body, but of late years we advise that chances for cure with radium are equal to that of hysterectomy; in addition there are no operative deaths. These conclusions we came to after careful follow-up of more than 50 cases of malignancy of the body of the uterus treated in our clinic with radium.

Adenomyomata are dangerous neoplasms when permitted to grow. According to Cullen a large majority of adenomyomata have their origin in the uterine mucosa, although they are usually found in the mid-layer of the uterine wall and are diffuse in character. Adenomyomata buried in the rectovaginal septum, a most favorable place for them, are most difficult to completely remove. The lack of a sac, and the almost uncontrollable hemorrhage, make the operation very taxing on both the patient and operator. Radium is safer than operation in some cases, and in case of tumor substance being left attached to the bleeding walls, radium, correctly screened, will prevent recurrence of the growth.

The first menstruation following intrauterine application of radium is often very profuse, if the radium is applied within five to seven days before the expected period. This is no doubt due to the stimulating effect of the rays which usually occurs within the first ten days after the radium is applied. There is at times reduction of the tumor before amenorrhea has been established, but oftener, the reduction is not marked before three to six months has elapsed. In our series of 287 cases, the number of menstrual periods varied from none to four. In only a few cases were there more than two periods.

Successful use of radium in non-malignant neoplasms of the uterus is largely de-

pendent upon the following factors: (1) accurate diagnosis; (2) properly selected cases; (3) correct graduation of dosage; (4) technique of application. We have found the result of radium uniformly satisfactory in 287 cases of benign uterine tumors. We were disappointed in but 9 cases. Two failed to receive sufficient radium, and 6 others were not given sufficient time before the surgeon operated. Another case had a very obstinate retroversion, which prevented sufficient radium being used to cause complete reduction of the tumor.

In our series of 287 cases, a vaginal discharge persisted for from three weeks to several months. The length of time of discharge was dependent on the size of the tumor. The discharge ceased in all cases eventually. There were no deaths. The minimum dose used was 400 mg-hr. and the maximum 4,800 mg-hr. Judging from publications of radium treatment for benign neoplasms of the uterus, one might expect about 33 per cent of all cases to be classed under radium treatment. In our Clinic which was conducted in private practice, 66 per cent were accepted for radium. This difference, I am sure, is due to the character of the patients applying for treatment. The Howard A. Kelly Hospital reports 75 per cent of all their cases of fibroids amenable to radium rays. The Kelly Clinic is a private clinic and a very large percentage of women seen there are more or less able to keep themselve in good physical condition and not so likely to permit uterine tumors to grow so large before being treated. The private practice clinic and not a large charity hospital clinic will see the larger number of radium cases.

The marked nervous manifestations following irradiation of the ovaries, sometimes referred to by gynecologists without experience in the use of radium, have failed to occur in our cases. Careful study of the history of those extremely nervous women will reveal marked nervousness previous to irradiation. Hot flushes were the most prominent and frequent symptom in our cases. The flushes were no more frequent nor severe than in the cases in which double ovariotomy had been performed. Again, the flushes and other nervous manifestations disappear, coincident with the return of menstruation, which does not occur after both ovaries have been removed.

Blood pressure readings were not aggravated. In many cases it was lowered temporarily when abnormally high, and the general symptoms referable to high blood pressure were lessened. There is usually a gain in weight which, however, is temporary, and can be controlled by diet, exercise and glandular therapy.

Discussion on Papers by Morton, Bowing et al., Corscaden, and Norsworthy

Dr. C. Jeff Miller, New Orleans, La. Since 1909 I have been using radium, and as I listened to the group of papers which have just been read, I found myself turning over in my mind the indications and contraindications for its use. They are well established by this time, as is the dosage of radium which it is wise and proper to use, and the most important thing for us to concentrate on now is the proper selection of cases, which means the proper diagnosis of cases. This is not always as simple as it sounds. As time passes, I find myself nothing like as positive in my opinions as I used to be; I have too often been in the wrong, too often had to change the entire plan of treatment which I had outlined.

To speak particularly of uterine fibroids, it is possible in private practice to treat some 30 per cent by irradiation, and I do not think that percentage can be safely passed. In public practice, at least among the negroes, irradiation is seldom possible. We see enormous fibroids in these women, very many of which are undergoing degenerations of various sorts, and we find chronic salpingitis, which of course strictly contraindicates irradiation, in from 70 to 90 per cent. Size, degenerations, pelvic infections, all combine to make the treatment of uterine fibroids in the negro woman a strictly surgical consideration.

We should remember that the use of radium is often radical and not conservative. It is certainly radical in the highstrung, nervous woman, who is inclined to have a stormy meno-

pause; in that type of patient, no matter what her age, surgery is truly conservative. In the young woman irradiation is never conservative, especially when we remember that a certain percentage of fibroids, certainly from 10 to 12 per cent, can be treated by myomectomy, with the conservation of future function. Its mortality, in the properly selected case, is not high, in 90 per cent of cases menstrual function is normal thereafter, and in from 20 to 30 per cent of cases conception and normal gestation and delivery can be looked for. If, however, myomectomy cannot be performed, in the young woman and the nervous woman we shall best consider the interests of our patients if we resort to hysterectomy, radical though it may seem.

Another contraindication of the greatest importance is the type of cervix to be dealt with. Leucorrhea is a rather constant sequel of irradiation, even in the properly selected case, but pyometra is a frequent sequel in the improperly selected case, the patient with the long, tortuous cervical canal. Here, again, the use of radium is unwise and dangerous. I am afraid of radium, too, when there are changes in the ovaries. I may have had an unusually unhappy experience with ovarian papillomata in association with uterine fibroids, but I have overlooked them in the past, and I always had reason to regret my error.

It is quite possible, if surgery cannot be performed at once, to use irradiation in growths larger than those which fall within the limits usually set, a three or a three and a half months' pregnancy, as a temporary measure to check hemorrhage, and I am aware of the good results which have been reported from certain clinics in the routine irradiation of larger growths. But most of us, I think, will follow Dr. Corscaden's warning and will transcend the standard limitations cautiously, if at all.

It cannot be too strongly emphasized that radium should never be inserted into the uterus for fibroids or for any other type of disease, without a preliminary curettage to establish the exact conditions present, to eliminate malignancy, and to remove pedunculated polyps and small submucous growths. This type of tumor is peculiarly prone to degeneration after irradiation, probably because of its defective circulation, and dangerous infections can follow disregard of this precaution.

Irradiation has a special field in the treatment of uterine hemorrhage in young women, but it is admittedly a small one. I have used it in a certain percentage of my own cases, but always as a last resort, always after every other measure, including repeated curettage, had failed. In a small number of instances I have found blood transfusions highly successful, though I cannot explain why, and I use this measure routinely before resorting to radium. The recent investigations in the field of endocrinology, and the notable work done by Novak, in particular, give us every reason to hope that in the future we can control the hemorrhages of functional origin by rational organic therapy, without the risk of destruction of function which even a small application of radium introduces.

In conclusion, I would point out again the importance of a correct diagnosis before radium is used. Malignancy is an ever-present menace, and the safety of the patient, regardless of her age, demands preliminary curettage, with microscopic examination of the uterine scrapings.

Dr. William P. Healy, New York City. In irradiating the large uterus, whether it contains a fibromyoma or not, it is a wise plan to apply a sufficient number of capsules of radium so that the length of the radium application will practically correspond with the length of the uterine cavity above the internal os. We feel that this is rather desirable in the large uterus because if we use two capsules in a tandem it irradiates only a small area in the uterus, and if you plan to use a large dose in such a uterus you are very likely to find resulting from this intense radiation a local burn or ulceration of the uterine wall, which may result in pyometra. In those cases, we have usually planned a string of three or four capsules. Furthermore, the treatment is limited to 650 or 700 mc-hr. for each capsule. If the growth is as large as a four months' gestation we will not give even with three capsules more than 1,800 to 2,100 mg-hr. of radium treatment, but we will add to this a high voltage roentgen cycle of four exposures which will be given subsequently. Any uterus apparently containing fibromyomata which is to be treated with radium should be subjected to a preliminary curettage, and if the interior of the canal is nodular and if the patient is beyond the menopause we believe, due to the fact that we cannot properly curette such a uterus, it should be removed surgically because of the possibility of overlooking carcinoma of the endometrium.

We have had several recurrences of bleeding

from fibromyoma due to the fact that a submucous tumor became a definitely pedunculated tumor within the uterine cavity and within a year or two the patient again began to bleed. In each instance by myomectomy we were able to remove the tumor and the patient ceased to bleed thereafter.

Dr. Morton's communication was very valuable and we are indebted to him for drawing our attention to the possibilities of improving our technique, and possibly thereby increasing the percentage of cures in cancer of the cervix uteri. For many years, on the gynecologic service in the University of California Hospital, they have routinely carried out the treatment of carcinoma of the cervix uteri with some type of radiation therapy combined with hysterectomy. I should have said, perhaps, a Wertheim hysterectomy combined with irradiation. As a result of this work they have been able to obtain these specimens for study, specimens that have been irradiated and then removed surgically. They have proved in their results what has been largely realized, that we do not cure cancer of the cervix uteri by a Wertheim hysterectomy when the lymph glands have been involved. Not one of their cases of this type survived five years. The fact that they do find cancer cells still present in the uterus in careful study of a large percentage of these cases would lead us at once to the question as to the adequacy of the radiation that had been used. Of course that is the crux of the matter entirely. It must be evident that it was not adequate because within 2 cm. of the cervical canal or the uterine cavity viable carcinoma cells were found. We have a perfect field for the application of radium in carcinoma of the cervix uteri. We can apply from below in the vaginal canal, and from above in the cervical and uterine canal and there should be no difficulty whatever so far as the uterus is concerned in giving a dose of radiation which will take care of the carcinoma. Our only problem is not to give a dose which will damage the rectum or the bladder or which will lead to distress in some other way. In our work at the Memorial Hospital we say in the cervix proper we can use safely from 8 to 10 skin erythema doses of radiation with radium and roentgen rays. That includes one roentgen cycle, high voltage. Carcinoma of the cervix we know is a relatively radiation sensitive lesion and if with the doses that are now being used in the favorable cases we are leaving active cancer we would find, I believe, in the 40 to 50 per cent of cases that survive five years evidence of local disease in the cervix, or some place in close proximity to the uterine cavity before such patients die, but that is not our experience. Probably without exception none of our early cases show any local recurrence. Therefore, we believe the irradiation takes care of the cancer in the uterus. Our patients die from metastases, and that means they were not early cases. They were early only in appearance and not so far as metastasis was concerned. I am of the opinion that we will always have a great difficulty in getting more than 75 per cent five-year cures in the early cases. This may vary from year to year in different clinics. Metastases are thrown out very early and while the growth often seems early it frequently is advanced. For instance, one of our cases with a very small lesion had hardly recovered from the effects of the irradiation before she started to expectorate blood. She had a carcinoma in the lung. Were there two primary growths, or was the growth in the lung metastatic? If the crux of the matter only depended upon what is found in the uterus it would be worth while to do the Wertheim operation and cure them. That is why irradiation has so largely superseded surgery. Certainly we can use enough radiation in the vagina, and in the cervix and in the corpus to take care of cancer that is still confined to the uterus. We believe that it is far more important, based upon our experience at the Memorial Hospital, to start the irradiation, except in the most favorable early cases, with the high voltage roentgen-ray cycle. We use one cycle and within ten days all the superficial infected, fungated surface will be cleared up and the lesion reduced down to a firm surface. Radium when then applied is much closer to the out-growing border of the carcinoma and the chance of local recurrence is greatly reduced.

In addition, we believe that by this method of approach, using the roentgen ray first and radium second, and about eight weeks later another high voltage cycle, we will do much to improve end-results, not to the early and favorable group but to Group III cases.

Dr. Albert Soiland, Los Angeles. I am unable to do justice to these three splendid papers in a brief discussion, but will take the liberty to refer to that part of the symposium dealing with malignancy.

Dr. Healy has so ably presented the present-day method of treating carcinoma of the cervix

that we can only add our endorsement. I am glad he mentioned the use of the large so-called preoperative course of roentgen irradiation. Our group in Los Angeles has advocated this method most ardently for years, not only in cancer of the cervix but in every patient with cancer where the possibility of a metastasis cannot be excluded. In our own Clinic this procedure is followed in all such cases before radium is used. I agree with Dr. Healy that by this method, followed by radium, we can change the picture presented by Dr. Morton in no uncertain manner. At a similar symposium in California two years ago, Dr. William J. Mayo, in discussion, stated definitely that patients with cancer of the cervix in any stage should be referred to the radiologist for treatment.

Dr. Charles L. Martin, Dallas, Texas. I would like to say a word about the etiology of benign uterine hemorrhage. We are all familiar with the various organic conditions described in the textbooks which give rise to hemorrhage, but only recently have we learned something of the type of bleeding uterus in which no clinical evidence of pathology is demonstrable. In such cases various diagnoses such as "uterine insufficiency," "fibrosis uteri," "subinvolution of the uterus," "metropathia hemorrhagica," "endometrial hyperplasia," "adolescent hemorrhage," "uterine fibroids," etc., are found on the hospital charts.

Wilfred Shaw collected a series of these cases a few years ago and produced evidence indicating that the hemorrhage is due to a functional imbalance between the ovary, the pituitary and possibly the thyroid. Few practicing physicians recognize this endocrine disorder as an entity and unfortunately many patients are subjected to surgery when a proper combination of endocrine therapy and irradiation might produce excellent results. I think more patients would receive radiation therapy if the diagnosis "uterine hemorrhage without demonstrable pathology" were brought into more general use.

Dr. J. T. Murphy, Toledo, Ohio. I have been much interested in this symposium, but several factors have been neglected. We have had a good many communications regarding contraindications to radiation therapy. I think in the main they are true for radium, but I do not believe they are contraindications for roentgen therapy. We have heard a lot about inflammation of the pelvis as a contraindication. I agree that this is true in radium, but not for fractional doses of roentgen radiation. A number have discussed surgical procedure, but no one said what operation they did. In my hospital 11.8 per cent of the cures of carcinoma of the cervix uteri are in those cervices left after partial hysterectomy. I think there is a problem in morbidity that is important, and that is the matter of sex function after irradiation and surgery. It is very difficult to get a sex history from these women, but I have tried it in the roentgen-ray cases and have found there is very little interference. If you take out the cervix and do a complete hysterectomy, you have to take off a portion of the vagina. You have then left a woman still in the sex age, with normal stimulation of the sex function, but with mechanical inability to satisfy it. This is the cause of some of the serious mental symptoms that follow surgery. I am speaking now in favor of the fractional dose of roentgen radiation in women of that age, and not of radium.

Dr. William H. Cameron, New York City. I wish to report two cases, with uterine hemorrhage, treated by hard gamma rays—"distant" radiation by a 2 gram radium element pack. These cases were considered inoperable and it also seemed unwise to attempt a uterine application.

Case I. This patient, aged fifty-eight, had severe uterine hemorrhages. Clinical diagnosis: Multiple fibroids with possible fundus carcinoma. Treatment: Three series, 30-day intervals, 10 cm. distance, 5 skin areas for a total of 165,000 mg-hr. Hemorrhage checked and general condition gradually improved. Eight months later patient had a slight secondary hemorrhage and, as the general condition was now very good, the uterus was removed. No difficulty whatever was encountered. The uterus contained many fibroid remnants and, at one point, a small, well-circumscribed area of carcinoma. Patient made a rapid recovery and now, three years later, is in excellent health. The interesting points in this case are: the ease with which the uterus was removed eight months after hard radiation therapy and that very sick patients stand this form of radiation.

Case II. This patient, aged eighty, had severe hemorrhages with rapid loss of weight. Clinical diagnosis: Fundus carcinoma. Treatment: During six days (10 cm. distance, 3 skin areas) 40,000 mg-hr. was given. The hemorrhage was promptly checked and the general improvement marked. Two years and six months later, the patient was in good condition. This case is interesting because it confirms Healy's findings

that some fundus carcinomas are very radiosensitive.

DR. C. R. CRUTCHFIELD, Nashville, Tenn. In 286 private cases we have used radium, out of some 563 fibroids of the uterus. In private practice 50.2 per cent of the cases were given uterine radium and 3 cases only were given a vaginal radium pack. In relation to the hemorrhage associated with infection in which operation is contraindicated, 3 were given vaginal packs, abdominal packs, without intrauterine radium applications. I think the intrauterine applications are contraindicated then, but if you use vaginal packs you can get by with those cases and can carry them over successfully. In these cases 75 per cent of the patients were more than forty years of age and 5 per cent were less than thirty-five years of age.

I think all the cases have been covered in regard to the contraindications for radium therapy except those of secondary anemia. In this group 20 per cent of the patients had blood transfusions. We gave no patient, except one, radium if the hemoglobin was less than 40 per cent. In that case we did not use a transfusion and against our better judgment used radium and she developed a temperature of 104° or 105° F. which persisted for a week or ten days. We thought we would lose her but fortunately the cervix opened up and a large amount of material drained out, following which the temperature became normal and she recovered.

In this series we lost only one case, from embolus, on the twelfth day. She developed a low grade pelvic peritonitis some four days after the intrauterine radium therapy, without any history of previous pelvic inflammatory trouble. When recovering from this, she then developed a pulmonary embolus and died before anything could be done.

In this series 50 per cent of the growths were reduced to half their size, and 35 per cent to practically normal size. We had 3 cases of pyometra develop in which we used dilatation and allowed to wear an indwelling pessary, which gave relief. Six patients (2.09 per cent) came to subsequent operation. In 4 of these at operation nothing was found except practically a normal-sized uterus with some very small fibroids in it. Two had recurrences of tumors. In one at operation we found an orange-sized fibroid in the broad ligament detached from the practically normal uterus.

In nervous women who fear cancer it may be better to use surgery. One case treated elsewhere and 3 of our own cases came to subsequent operation because of cancerphobia.

Another patient, eighteen months after irradiation, developed a tumor which grew rapidly until it reached the size of a four months' pregnancy. We feared malignancy and this was operated upon but no malignancy was discovered, only a rapidly growing fibroid.

In our series of 286 fibroids we found on diagnostic curettage 3 cases of carcinoma of the body of the uterus which were so treated.

Another point is that in cases in which there is no definite fibroid present, as Dr. Morton brought out, the patients should be subjected to careful examination to see if there is any hypertension or endocrine dyscrasia. We ran a metabolism test on all of these and by carrying out proper glandular therapy in those with low metabolic rates we have relieved them considerably. This applies more to patients below thirty years of age.

For fibroid uteri in patients approaching the menopause, in which we have done a diagnostic curettage, radium therapy is indicated when their only symptom is hemorrhage. I think we can sum up by stating that radium is the treatment of choice in menorrhagia associated with uncomplicated fibromyomata less in size than three and one-half months' pregnancy in women approaching or within the menopausal years, or of a fibrous uterus possibility of malignancy is eliminated by curettement.

DR. M. LENZ, New York City. Dr. Corscaden's paper represents a well-substantiated answer to the criticism of other operating gynecologists who state that long continued follow-up of fibromyomata of the uterus treated by irradiation is missing.

DR. MORTON (*closing*). Dr. Healy was very kind in his discussion but I disagree with him in his remarks regarding recurrences in Groups I and II which we find reported in all series. He said it was their experience that they came in the manner of glandular metastases, that in their hands all local cancer was undoubtedly destroyed by radiation. My reasons for disagreeing with this point of view are that the method of irradiation which we employed gave 38 per cent five-year cures, which is almost as high as the 44 per cent of the Memorial Hospital series. That places the method, while perhaps not ideal, as one that is roughly equivalent to those in use elsewhere, yet cancer was found in approximately 50 per cent of cervices so treated. Parenthetically, I think it well worth

while to re-emphasize that the clinical absence of carcinoma after irradiation may deceive one markedly.

Apparently we have not had the same experience in regard to metastases, as indicated in the surgically treated cases in which recurrences did not occur after operation. There was no dissection of glands except where enlarged ones were found, yet these cases once they got by primary mortality, continued alive in the large percentage of cases. The experience we have had with recurrent carcinoma of the cervix is that it is a local recurrence. I do not mean that cancer necessarily recurs in the portion of the cervix which is visible but often does recur in those portions which extend out from side to side to merge into the parametria. Certainly many women die of advanced cervical cancer in whom no glandular metastases have been revealed, even in these advanced cases.

In regard to the possible reasons for inadequacy of irradiation, it seems to me it is not so much improper amount as improper placing of radium which is all important.

Regarding operation, the mortality in Dr. Lynch's series was 12.9 per cent, but we feel that the primary mortality has probably been due to operating upon cases which should not have been subjected to surgery. In the last 40 cases, there have been no deaths. It occurred mainly in cases in which cancer had extended beyond the cervix into the parametrium. As to doing wide dissection, I cannot help feeling that for uterine cancer the day of extension of anatomical fields is about over. If the cancer can be cured, it can be accomplished by a reasonable type of procedure which is not necessarily the most radical.

Dr. Desjardins (closing). In connection with fibromyoma, we radiologists must share with the surgeon a great responsibility in regard to the patient. I thoroughly agree with the remarks of Dr. Miller and Dr. Corscaden regarding the necessity of thorough examination. There is no question that, in different parts of the country, many carcinomas have been irradiated on insufficient diagnosis. For this reason, therefore, the results cannot be included in careful statistics.

Dr. Murphy's point that the contraindications mentioned in our paper related to radium is well taken but does not apply so much to roentgen therapy. In the postmenopausal or menopausal group certain points should, at least in certain cases, be considered more seriously than they often are. Since diagnosis is the main point, as in every medical problem, there is no question that diagnostic curettage must be made in every doubtful case, and whenever this is done it is not only proper but wise to apply radium so that the patient will not be subjected to two different procedures. In other cases the advisability of intrauterine radium application is not so clear. Unless the necessity for diagnosis is definite, and unless better results can be obtained, it is certain that the average patient would prefer to avoid intrauterine treatment if possible. This can be accomplished by external irradiation. I have heard it said that internal irradiation brings about quicker results than external irradiation. That has not been my experience. In most cases, whether treated by radium or roentgen rays, the patient usually has one period, or sometimes two periods, after irradiation, and that is usually the end of it. Moreover, in something over 50 cases where we have used external irradiation alone, treatment was repeated in but 2 cases. In one instance this was because the patient was so apprehensive about bleeding that we gave a second course of treatment to quiet her fear.

In patients weighing not over 150 pounds our method is to expose for sixty minutes two fields, one anterior and one posterior, to rays generated at 200 peak kv., filtered through 0.75 mm. of copper and 1.0 mm. of aluminum, at a focal-skin distance of 50 cm. In patients weighing over 150 pounds we use two anterior fields 10×15 cm. and one posterior field 20×20 cm.

In the group mentioned by Dr. Martin, where no lesions are found to account for the disturbance, endocrine disturbance may play a part. We have tried pituitary irradiation in a small group of cases. Some patients have been improved, some have shown slight improvement, and some no improvement whatever. Our series is too small to warrant more definite statements. At the present time the value of pituitary irradiation depends on the selection of cases, and this is still an uncertain factor.

Dr. Corscaden (closing). I am glad to see so much discussion concerning benign cases for the disability from benign lesions is of great importance. I think if I summed up the treatment I would say it would be about 90 per cent gynecologic and 10 per cent radium technique.

It may help to give you a formula which we use in approaching one of these cases. We divide the problem into three stages; first, the question of hemorrhage; second, the question of di-

agnosis; third, the question of the later effects of the irradiation. Hemorrhage in our minds comes from three causes. Every woman menstruates every twenty-eight days if she is in health, and I do not think it is necessary to stress the weirdness of this endocrinological influence. From the various elements that figure in our research clinic there are probably eight endocrinological substances. At least two from the pituitary, two we discover in the ovary, and the rest of them are very hazy but assumed because of different effects which different treatment produces. The second is bleeding from a disease process, trauma and ulceration and so on. The third is pregnancy. If a woman comes in bleeding she has one of these three. The second point in the diagnosis is the question of growth. We decide whether there is anything in that growth which menaces life. We do not fear the lighting up of old inflammatory lesions. We have used roentgen therapy in cases with adhesions so marked that the tumor could not be removed, and the fibroids disappeared with no harm to the patient. Whatever evidence we have is that the radium does not do damage, or the roentgen ray, but the radium slough is a good portal of entry for any infection. I have the feeling that when my cases become infected the causes of infection lie in the causes of any other infection.

The other question is of the adnexal tumors. We have had 4 of these cases in which tumor developed following irradiation. There has not been a single cystic ovary. It is my opinion that any corpus luteum cysts will shrink, and I have 2 cases to bear this out. One woman was operated upon for dysmenorrhea with cystic ovaries. Since the pain continued we gave roentgen therapy and the masses on both sides disappeared. In another case after a supravaginal hysterectomy, an ovarian cyst appeared; we used roentgen therapy and it disappeared. Neoplasms of the ovary may occur following radiotherapy but not so-called cystic ovaries.

We often do a curettage, use no radium whatsoever, and accomplish our purpose by the use of roentgen rays when the canal is long and tortuous.

If a woman is psychoneurotic following the artificial menopause it will be about 90 per cent because of the ordinary causes of psychoneurosis and about 10 per cent because of endocrine disturbances. Seventy-five per cent of the women have been less nervous following the menopause than before. They feel so much better generally that whatever irritability may have been the result of the radium therapy is more than counterbalanced. Treat the women psychologically before the treatment, re-educate them regarding sex matters before the therapy. Since 1920, when we adopted this plan, we have had no trouble with psychoneuroses. They are psychic and not endocrinological disorders.

Dr. Norsworthy (closing). Regarding the European treatment, I visited all of the cancer clinics in Europe two years ago, and found radium and roentgen therapy in general use, except in Germany and Austria, where they were unable to purchase the necessary equipment. One of the speakers said if the tumor did not disappear within three or four months, radium was a failure. That statement I believe not well founded. In some cases we repeat radium treatment at the end of three months, and even in the large fibroids we have repeated it at the end of six months, after which the tumor entirely disappeared. The large tumors had best be removed by operation, if not contraindicated. The average death rate from radical myomectomy is about 15 per cent, as estimated from the clinics in the United States and Europe; and that risk should be considered in deciding the treatment to be used. Vaginal packs of radium may be essential when one cannot enter the uterine cavity. However, when the tumor has interfered with the uterine canal so that a radium applicator cannot enter without laceration, I would consider it an unfavorable case for radium therapy. The abdominal application of radium should be accompanied by roentgen therapy in very large tumors.

The glandular treatment in women passing the menopause cannot be overestimated, and must be worked out carefully.

In regard to cancer of the body of the uterus, we have 3 living cases that were opened and closed as inoperable and hopeless by surgeons of experience. One patient is alive after two and a half years, one alive after four years, and one alive after seven years. All three are free from any evidence of cancer, and are apparently well.

The uterus should be carefully measured, and the radium applicator arranged so that the rays will be distributed where most needed, and throughout the uterine cavity. To repeat, use plenty of radium correctly screened and correctly placed, for best results. We anesthetize and curette and do a biopsy in every case if in doubt as to diagnosis.

CONGENITAL ATRESIA OF THE ESOPHAGUS WITH TRACHEO-ESOPHAGEAL FISTULA

CASE REPORT

By J. FRIEDMAN, M.D.
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Baby W., male, born at full term, weighing 7 pounds, was admitted to the hospital when two days old. At birth, there was no cyanosis nor difficulty of breathing. There was noticed a copious discharge of white frothy fluid from mouth and nose, which persisted. When fluids were given by mouth there was immediate regurgitation, followed by coughing and cyanotic attacks. The infant was unable to retain anything by mouth. Atresia of the esophagus was diagnosed clinically. Besides the above anomaly there were also deformities of both external ears. No external auditory canal could be demonstrated on the left side.

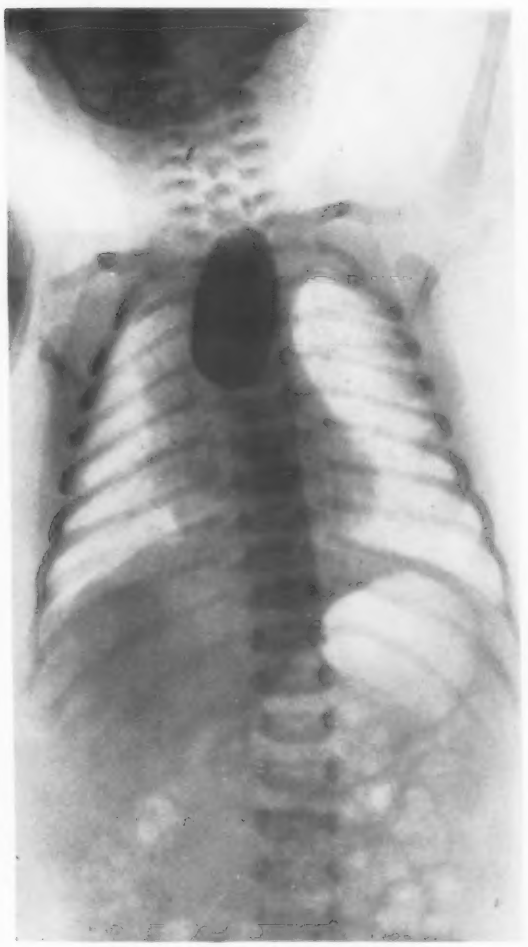

FIG. 1

FIG. 2

Under the roentgenoscope the barium fluid given by mouth stopped permanently in a blind pouch at the level of the 4th dorsal vertebra (Fig. 1). The lateral view (Fig. 2) shows the filled upper esophagus pressing the trachea forward and compressing it. There is a moderate amount of air or gas in the stomach and intestine.

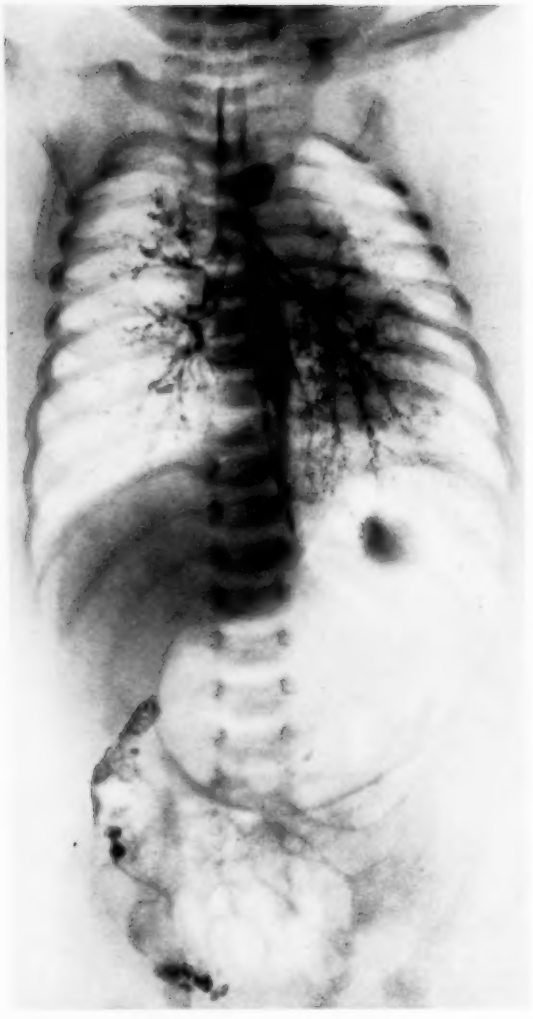

Fig. 3

Four days later there is still a small residue of barium found in the esophageal pouch. The stomach and intestine contain a large amount of air. Patches of barium are visualized in the proximal colon. The film taken before the lipiodol filling and demonstrating it clearly is not reproduced, but the barium in the colon can be seen in Figures 3 and 4.

Under roentgenoscopic control, with the infant lying in the prone position, 2 c.c. of lipiodol was injected by intratracheal intubation, the soft rubber tube being introduced to slightly above the bifurcation. The lipiodol first filled the left bronchial tree, then at the same time it passed down the lower segment of the esophagus into the stomach, and finally filled the right bronchial tree. As seen in Figures 3 and 4, the lower esophageal segment is inserted into the posterior tracheal wall slightly above the bifurcation. The fistula is situated to the left of the carina and about one-half inch from the upper esophageal pouch.

The parents refused to permit a gastrostomy. The baby died when eight days old.

Synopsis of Autopsy Record. The autopsy was done by the Hospital pathologist six hours after death. The upper esophageal segment represented a dilated blind pouch, 4.5 cm. long and 1.5 cm. in diameter. The lower esophageal segment was not dilated. It extended up from the cardiac ring in its normal position for a distance of 4 cm. It then tapered to a small oblique opening, 0.8 cm. in diameter, into the trachea.

Fig. 4

This opening was situated just to the left of the point of branching of the trachea to form the left main bronchus. On its posterior surface there was thus produced a tracheo-esophageal fistula. There was obviously no communication between the upper and lower esophageal segments which were 1 cm. apart (see Fig. 5; *a* represents the ventrodorsal view, *b* the dorsoventral view, and *c* the lateral view of the pathological specimen). No anomalous branching of right or left bronchi could be demonstrated.

Other congenital anomalies in this case included: (1) a true diverticulum (Meckel's) in the lower ileum, 50 cm. above the ileocecal valve; (2) a persistent tubercle just in front of the tragus of either auricle; (3) complete absence of the left external auditory meatus. Death was due to a terminal respiratory infection.

a *b* *c*

FIG. 5

Discussion. This case report is submitted as one of peculiar clinical interest, not because of the congenital esophageal atresia with tracheal fistula (this is a well-recognized, not too uncommon anomaly), but because the developmental defect was so readily and accurately demonstrated roentgenologically during life.

I wish to thank Dr. M. Scherzer, in charge of the Pediatrics Department for permitting the publication of this case, and Dr. W. H. Chase for contributing the autopsy report.

CHARCOT'S DISEASE OF THE ELBOW JOINT

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CHARCOT'S disease of the elbow joint is apparently quite uncommon. Charcot[1] does not mention the elbow in his treatise on the arthropathy, except that if the arthropathy does occur in the upper extremity tabes dorsalis would be late in the lumbar region of the cord. Wile and Butler[2] report 72 cases of Charcot joints in which one was of the elbow joint. It was mentioned as one case in five found in other joints. The neurological textbooks of Church and Peterson,[3] Dana,[4] Starr,[5] and Mettler,[6] say that the elbow joint may be affected but give no indication that they have seen any cases. Young[7] in his "Manual and Atlas of Orthopedic Surgery" quotes Bradford and Lovett as having found 10 cases in 107 Charcot joints; he also quotes Chepault as having reported 217 Charcot joints, none in the elbow joint. In two editions of Bradford and Lovett's book I find no reference to the 10 cases of Charcot elbow joints. Whitman[8] quotes Schlesinger as having reported 24 in 97 cases of Charcot joints. Kocher[9] reports one case of Charcot elbow joint. Baetjer and Waters[10] state that Charcot joints in the upper extremities are probably due to syringomyelia, since weight bearing plays an important rôle in the production of a Charcot joint of tabes dorsalis.

FIG. 1. Case 1. Roentgenogram of elbow of patient with syringomyelia shows marked sclerosis of the humerus, small amount of subluxation, destruction of the articular surfaces and new bone formation. The latter is more organized than in the other cases.

The roentgen appearance of Charcot's disease of the elbow joint is not unlike Charcot's disease in the lower extremities. The elbow joint being quite rarely involved might cause some difficulty in diagnosis; however the "bag of bones" appearance is present. The joint shows marked soft tissue swelling, destruction of the articular surfaces, disorganization and large irregular calcified masses scattered throughout the joint area.

It would seem unwise from these cases to call them all Charcot joints from tabes dorsalis. There seems to be no difference between the case of syringomyelia and tabes dorsalis from the roentgen standpoint.

CASE REPORTS

CASE 1 (No. 1157265). J. H., male, aged forty-nine, laborer, entered the Cook County Hospital March 4, 1930, complaining of swelling of the left elbow for two years and impair-

ment of function of the left hand for three months. The swelling had become worse in the last year. About five months ago his hand became cold and in the last two months he had lost strength in his hand.

The essential physical findings were: No Argyll-Robertson pupil, patellar reflexes exaggerated, testicular sluggish, cremasteric absent and the abdominals absent.

The left elbow was markedly swollen and fluctuant. Bone crepitus could be felt and the forearm was cold. Marked subluxation of the elbow joint and no pain on motion.

Neurological examination showed evidence of a Charcot joint without signs that would suggest syringomyelia or tabes dorsalis. In the absence of trophic disturbances, atrophies, peripheral hypesthesias usually of the segmented type, the diagnosis was more probably tabes dorsalis in spite of the negative serological examination. The patient was discharged without treatment.

Case II (No. 1160303). M. N., male, aged

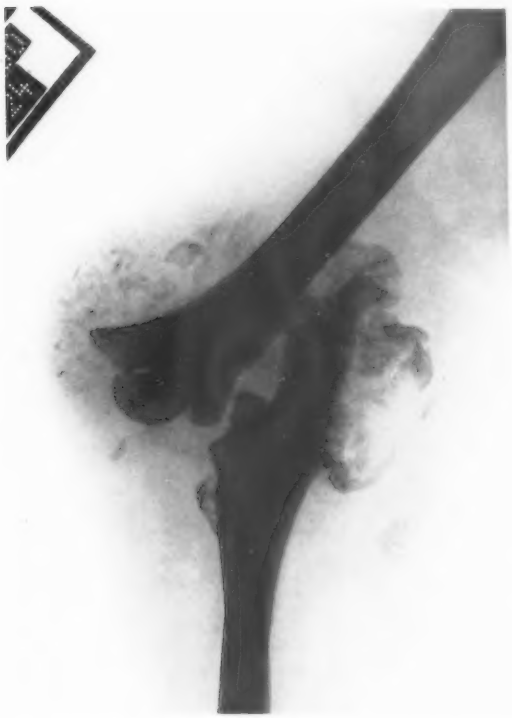

Fig. 2. Case II. Roentgenogram of elbow of patient with tabes dorsalis shows a large soft tissue tumor, irregular formation of new bone, complete dislocation and comparatively little destruction of the articular surfaces.

Fig. 3. Case III. Roentgenogram of elbow of patient with syringomyelia shows marked disintegration of the joint, subluxation, soft tissue tumor, irregular distribution of new bone, dislocation of the condyle of the humerus and destruction of the articular surfaces of the joint.

twenty, was admitted to the Cook County Hospital March 25, 1930, as an attempted suicide. His right elbow started to swell three and one-half months previously and twenty-four hours previously he fell out of bed injuring the elbow. He admitted syphilis followed by treatment.

The essential physical findings were: Argyll-Robertson pupil, incoordination, marked hypotonia, diminished sensation over both lower extremities and reflexes absent.

The right elbow was markedly swollen, boggy, not painful and no redness. Marked bone crepitus and increased motion. Serological examination negative. No treatment advised.

Case III (No. 1223970). T. B., male, aged fifty-two, laborer, was admitted to the Cook County Hospital on May 9, 1931, complaining

of swelling of the right elbow for two weeks and difficulty in walking for seven years.

The essential physical findings were: No Argyll-Robertson pupil, bilateral ankle clonus, Babinski and patellar clonus.

The right elbow showed a large, red, hot, swollen, bone-hard tumor, with marked increase in motion and no pain. Bone crepitus and subluxation of the joint. Serological examination negative. The neurological examination suggested the Charcot joint of syringomyelia. The patient presented a segmented type of anesthesia and increased reflexes indicative of a pyramidal tract lesion.

The patient's arm was amputated since it was entirely useless.

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Vol. XXIX, No. 4

THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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Publisher: Charles C Thomas, 220 East Monroe St., Springfield, Illinois

Issued Monthly. Subscription $10.00 per year, $11.00 in Canada and $12.00 in foreign countries. Advertising rates submitted on application: Editorial office, 110 Professional Building, Detroit, Mich. Office of publication, 220 E. Monroe St., Springfield, Ill. Information of interest to all readers will be found on page iv.

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EDITORIAL

MODERN ALCHEMY

SEVERAL hundred years ago the science of chemistry began as a series of attempts to transmute base metals into gold and other precious metals. All those attempts of honest men and of charlatans, who were far in the majority, proved to be fruitless. Thus arose the great principle of the finality and immutability of the atom as the ultimate unit of matter. For more than a hundred years chemistry and physics were built up around the concept of the indivisibility and permanent stability of atoms. This fundamental concept has remained down into the memory of all of us.

The ultimate permanence of atoms of course received a serious blow with the discovery of radioactivity or the process of spontaneous breakdown of some of the heaviest atoms whose hearts or nuclei were so complicated as to be unstable. And yet, here again man seemingly was helpless by his puny methods to affect in any way the process of radioactive disintegration. The forces and energies involved seemed far beyond the power of any man to produce or control.

Now upon the world's stage we look upon a most astonishing state of affairs. Chemists and physicists have become alchemists in the direct sense of the word, as they have discovered from long persistent inquiry that, after all, these atomic hearts are vulnerable to bombardment. Man has within his power to control and utilize infinitely small projectiles of unbelievable energy and velocity.

Only a few short months ago we could write down as the fundamental unit particles from which the universe is constructed the following:

The *electron*, or the unit of negative electricity.

The *proton*, or the heart of the hydrogen atom with a single positive charge and a mass slightly greater than one as compared with the mass of the oxygen atom considered as sixteen.

Everything material in the whole universe thus was to be considered built up from the proper combination of electrons and protons. For example, the oxygen atom has a minute nucleus in which the mass is concentrated, built from sixteen protons, held together by eight electrons, while around this nucleus as a sort of planetary system are to be found eight outer electrons. To these two unit fundamental particles might be added the *alpha particle* produced by radioactive atoms, which is really the heart of a helium atom and which acts apparently as a stable unit in itself although obviously consisting of four protons condensed together to form the helium nucleus; and the *photon*, or the unit particle of radiation as distinguished from the wave properties of radiation which is, in a sense, only a non-material messenger of the proton and the electron.

Very few people ever dreamed that there could be found or even that there existed any other fundamental units since these seemed to be adequate to explain matter and radiation energy. But now in 1933, behold the list of fundamental ultimate building stones of the universe:

The *negatron*, formerly called the electron.

The *positron*, a single unit positive charge of electricity dissociated from mass.

The *neutron*, a close-coupled positive and negative charge giving a particle of neutral charge.

The *proton*.

The *alpha particle*.

The *photon*.

The discovery of the neutron and the positron came as a result of attempts to transmute one chemical element to another by bombarding atomic nuclei with alpha particles from radioactive materials, or with high speed protons. A little more than a year ago Bothe and Becker, working in the German Reichsanstalt discovered that some kind of very penetrating rays, supposedly like the therapeutic gamma rays, or roentgen rays of short wave length, were emitted when beryllium atoms, especially, were bombarded by alpha particles from polonium. The phenomenon was further studied by Curie and Joliot in the Paris Radium Laboratory. It remained, however, for Chadwick and his coworkers in the Cavendish Laboratory in England, under the direction of Sir Ernest Rutherford, to demonstrate that these penetrating rays are electrically neutral and are *neutrons*, which are produced by a reaction like this:

$$\text{Beryllium}^{9} + \text{Helium}^{4}\ (\alpha) \rightarrow \text{Carbon}^{12} + \text{Neutron}^{1}$$

These neutrons, produced by bombardment, are in turn capable of acting as disrupting projectiles, for when one of them collides with the nucleus of a nitrogen atom this nucleus is shattered into boron and helium atomic nuclei, whose tracks may easily be identified. Similarly if these neutrons pass through any material containing hydrogen, such as paraffin wax or water, protons are ejected.

The discovery of the positron, or positively charged twin sister of the negative electron, was announced by Professor Anderson of the California Institute of Technology a short time ago. Only a few days ago its presence in cosmic rays was confirmed in the Cavendish Laboratory by Blackett.

In addition to the sensational discovery of these two new fundamental entities, the neutron and the positron, remarkable alchemical feats are being performed today in which the familiar proton serves as the projectile. No less remarkable than the fact that protons moving at high speeds can disrupt atomic nuclei and change one element to another are the ingenious methods by means of which these protons can be given enormous kinetic energies, up to 1,500,000 electron-volts so far.

Cockroft and Walton in England were the first to devise an artificial production of fast protons. A few months ago they bombarded lithium with these protons, and identified the products of the disintegration as alpha particles or helium nuclei:

$$\text{Lithium}^{7} + \text{Hydrogen}^{1}\ (\text{proton}) \rightarrow 2\ \text{Helium}^{4}\ (\alpha)$$

Of course these processes are not efficient in the sense of producing large quantities of a new element. Cockroft and Walton found that one alpha particle was produced for every billion protons at 250,000 volts. It has remained for American physicists at the University of California, Doctors Lawrence, Livingston, Henderson and White, to improve greatly the experimental technique so that protons with energies up to a million and a half electron-volts are produced and used in the disintegration of lithium, boron and other elements. In their ingenious apparatus, looking like a kind of pill-box cut in two, protons from a filament in hydrogen gas are kept circling around in a magnetic field between two series of plates, with oscillating potential, so that the initial 4,000 volts accelerating force is augmented each time the proton crosses from one series of plates to the other, up to the million or more electron-volts. These energetic hydrogen hearts are then shot at a target, with the result that lithium or boron atomic nuclei cannot endure the onslaught. The effort has been made to give these projectiles greater and greater energies. It remained for some German investigators recently to show that disintegration can occur with protons with energies even as low as 29,000 electron-volts.

Only a few days ago Tuve and Hafstad at the Carnegie Institution in Washington accomplished another transformation of unusual interest. They found that

$$\text{Aluminum}^{27} + \text{Helium}^{4} \quad (\alpha) \rightarrow \text{Silicon}^{30} + \text{H}^{1}$$
(proton)

However, this took place only if the alpha particles were very carefully "tuned" to the aluminum atoms, or had just the right amount of energy (600,000 volts) to penetrate or set into resonance the aluminum atomic hearts.

And so in the light of these amazing developments in research of the past few months, who can say that science is finished, and that everything of any importance has been discovered? In spite of the darkest days in economic history, surely these are great times in which to live. We are coming daily to a clearer knowledge of the universe, and to appreciation of the greatness of men's minds which can conceive such experiments and interpret them unmistakably in terms of the utterly smallest things in the universe. Certainly it is an overpowering inspiration to contemplate the fact that by mixing a little radium or polonium or emanation, so familiar to roentgenologists, with a little powdered beryllium in a test tube, we are producing invisible, infinitely small projectiles, so powerful, with such terrific velocities, that the nuclei of atoms, seemingly among all things the most truly everlasting and unchanging, can be shattered. Nineteen thirty-three has seen the return of the alchemist—but the most advanced and brilliant modern scientist, who gives not a thought to changing lead to gold so as to become magically wealthy, but to achievements infinitely more priceless and spectacular.

George L. Clark

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. E. P. Pendergrass, University Hospital, Philadelphia, Pa.
Annual Meeting: Chicago, Ill., Sept. 25–30, 1933.

American College of Radiology
Secretary, Dr. Albert Soiland, 1407 S. Hope St., Los Angeles, Calif.
Annual meeting: Chicago, Ill., Sept. 25–30, 1933.

Section on Radiology, American Medical Association
Secretary, Dr. J. T Murphy, 421 Michigan St., Toledo, Ohio.
Annual meeting: Milwaukee, Wis., June 12–16, 1933.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y.
Annual meeting: Chicago, Ill., Sept. 25–30, 1933.

Radiological Section, Los Angeles County Medical Society
Secretary, Dr. D. R. MacColl, 2826 S. Hope St., Los Angeles, Calif.
Meets on the third Wednesday of each month at the California Hospital.

Radiological Section, Southern Medical Association
Secretary, Dr. C. H. Heacock, 20 S. Dunlap St., Memphis, Tenn.
Annual meeting: Richmond, Va., November, 1933.

Brooklyn Roentgen Ray Society
Secretary, Dr. G. W. Cramp, 921 President St., Brooklyn, N. Y.
Meets monthly on first Tuesday, October to April.

Buffalo Radiological Society
Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St., Buffalo, N. Y.
Meets second Monday of each month except during summer months, place of meeting selected by the host.

Chicago Roentgen Society
Secretary, Dr. George M. Landau, 660 Groveland Park.
Meeting second Thursday of each month October to May inclusive at Virginia Hotel.

Cincinnati Radiological Society
Secretary, Dr. H. G. Reineke, Christian R. Holmes Hospital, Cincinnati, Ohio. Meetings held monthly.

Cleveland Radiological Society
Secretary, Dr. M. A. Thomas, Medical Arts Bldg.
Meetings are held at 6:30 P.M. at the Cleveland Chamber of Commerce Club rooms on the fourth Monday of each month from October to April, inclusive.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. R. Witwer, Harper Hospital.
Meets monthly on first Thursday from October to May, at Wayne Country Medical Society Building.

Florida Radiological Society
Secretary, Dr. W. McL. Shaw, 418 St. James Bldg., Jacksonville, Fla
Meetings held twice a year, May and November.
Next meeting, Hollywood, Fla., May 1, 1933.

Illinois Radiological Society
Secretary, Dr. L. M. Hilt, Myers Bldg., Springfield, Ill.
Regular meetings held quarterly.

Indiana Roentgen Society
Secretary, Dr. J. N. Collins, Indianapolis, Ind.
Annual meeting each February 22 in Indianapolis.

Michigan Association of Roentgenologists
Secretary, Dr. S. W. Donaldson, St. Joseph's Mercy Hospital, Ann Arbor, Mich. Three meetings a year, Fall, Winter, and Spring. Next Meeting, University Hospital, Ann Arbor, Mich., May 27, 1933.

Milwaukee Roentgen Ray Society
Secretary, Dr. J. E. Habbe, 221 Wisconsin Ave., Milwaukee, Wis.
Meets first Friday in October, December, February and April. Place of meeting designated by the president.

Minnesota Radiological Society
Secretary, Dr. L. G. Rigler, University Hospital, Minneapolis, Minn. Next meeting, Rochester, Minn., May 22, 1933.

New England Roentgen Ray Society
Secretary, Dr. Thomas R. Healy, 370 Marlboro St., Boston, Mass.
Meets monthly on third Friday, Boston Medical Library.

New York Roentgen Society
Secretary, Dr. C. W. Schwartz, 33 E. 68th St., New York.
Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

Central New York Roentgen Ray Society
Secretary, Dr. H. S. Bull, 604 Masonic Temple, Auburn, N. Y.
Three meetings a year—January, May and November.

Pennsylvania Radiological Society
Secretary, Dr. W. E. Reiley, Clearfield, Penna.
Annual Meeting, Penn-Alto Hotel, Altoona, Pa., May 24–25, 1933.

Philadelphia Roentgen Ray Society
Secretary, Dr. Karl Kornblum, 3400 Spruce St.
Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thomson Hall, College of Physicians, 19 S. 22d St.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. W. W. Fray, Strong Memorial Hospital.
Meets monthly on second Thursday from October, 1932, to May, 1933 inclusive, at 7:45 at the Rochester Medical Association Building.

St. Louis Roentgen Club
Secretary, Dr. W. K. Mueller, University Club Bldg.
Meets first week of each month. Time and place of meetings designated by president.

South Carolina X-Ray Society
Secretary: Dr. R. B. Taft, 105 Rutledge Ave., Charleston, S. C.
Meets at time and place of South Carolina State Medical Association. Next meeting, Spartansburg, April, 1933.

Texas Radiological Society
Secretary-Treasurer, Dr. C. P. Harris, Houston, Texas.
Meets annually one day preceding the meeting of the Texas State Medical Association.

University of Michigan Roentgen Ray Society
Secretary, Dr. C. C. Taylor, University Hospital, Ann Arbor, Mich.
Meets first and third Wednesday evening of the month from October to June, at 8 o'clock in the amphitheatre of the University Hospital.

*Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

Virginia Roentgen Ray Club
Secretary, Dr. Wright Clarkson, 205 S. Sycamore St., Petersburg, Va.
Meets annually in October.

Cuba

Sociedad Cubana de Radiologia y Fisioterapia
Secretary, Dr. Luis Fariñas, Animas 110, Havana, Cuba.
Meets monthly in Havana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets on the third Thursday of each month, from November to June inclusive, at 8:15 p.m., at 32 Welbeck St., London, W. 1., or as advertised.

Electro-Therapeutic Section of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:30 p.m. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Colin Macdonald, Lister House, 61 Collins St., Melbourne, Australia.
Meets monthly at Melbourne during the winter.

Section on Radiology, Canadian Medical Association
Secretary, Dr. A. H. Rolph, 160 St. George St., Toronto, Ont.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. P. C. Fenwick, The Hospital, Christchurch. Meets annually.

Continental Europe

Belgian Society of Roentgenology
Secretary, Dr. J. Boine, Avenue des Allies, 134, Louvain, (Belgium).
Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Societe de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel.
Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale
Meets monthly on fourth Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, 11/52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April in different German cities, at least once in five year in Berlin. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.
Permanent secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the Spring, and one in the Fall.

Societa Italiana Radiologia Medica
Secretary, Professor M. Ponzio, University of Turin, Turin.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Maracine 30 Bucarest, Rumania.
Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR, in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson.
Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin.
Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky.
Meets monthly on the first Monday at 8 o'clock, the place of meeting being selected by the Society.

Polish Society of Radiology
Secretary, Dr. Jan. Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. B. Krynski, 11 Zielna St.
Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime.

Society of Medical Radiology of Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. H. Scheuermann, Copenhagen.
Meets on the second Wednesday of each month from October to July in Copenhagen, at 8 o'clock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Society of Roentgenology
Meets first Tuesday each month, October to July.

Orient

Japan X-ray Association
c/o Orthopedic Surgery, Tokyo Imperial University
Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike, Kyoto, Japan. Meets bi-monthly on third Sunday.

PRELIMINARY PROGRAM OF THE AMERICAN CONGRESS OF RADIOLOGY*

September 25–30, 1933

Monday, 9:00 A.M., September 25, 1933.

Address of Welcome by President of the Chicago Medical Society, Austin A. Hayden, M.D.

Address by the President of the Exposition, "A Century of Progress," Rufus C. Dawes.

Address by the Surgeon-General of the United States Public Health Service, Hugh S. Cumming, M.D.

Address by the Editor of the Journal of the American Medical Association, Morris Fishbein, M.D.

Intermission—15 Minutes

Address by the President of the American Congress of Radiology, Henry K. Pancoast, M.D.

Address by the Executive Director, American College of Surgeons, Franklin H. Martin, M.D.

Address, "Radiosensitivity of Tumor Tissue," James Ewing, M.D.

Brief Reports of Committees—Special Announcements.

(Note: Following the opening meeting, the special committee meetings of the various component radiological societies will be announced by the officers of the societies, and may take place some time after adjournment each day.)

2:00 P.M.—Adjournment

Tuesday, 9:00 A.M., September 26, 1933.

Section "A," General Group of Papers devoted to CHEST DISEASES

"The Roentgen-ray in the Study of Pathology o Pulmonary Tuberculosis."

H. Kennon Dunham, M.D., Cincinnati, Ohio.

"Correlation of Clinical and Roentgenological Observations in Pulmonary Tuberculosis."

Lawrason Brown, M.D., and Mr. Homer L. Sampson, Saranac Lake, N. Y.

"Tuberculosis in Children."

F. Maurice McPhedran, M.D., Philadelphia, Pa.

"The Roentgen Examination of the Heart: A Critical Study of the Frontal Silhouette."

Fred J. Hodges, M.D., and C. B. Peirce, M.D., Ann Arbor, Mich.

"An Analysis of a Group of Primary Carcinomas of the Lungs, Treated with Deep X-ray Therapy."

Willis F. Manges, M.D., Philadelphia, Pa.

"Where is the Diaphragm?"

William H. Stewart, M.D., and H. Earl Illick, M.D.

11:00 P.M.—Recess

"Lymphoblastoma of the Chest and Elsewhere."

George W. Holmes, M.D., Boston, Mass.

"Roentgen Diagnosis of Interlobar Pleurisy." (Lantern Slides.)

Charles A. Waters, M.D., Baltimore, M.D.

"Accessory Sinus Diseases in Relation to Chest Diseases."

W. Walter Wasson, M.D., Denver, Colo.

"Non-Tuberculous Inflammation of the Lungs."

W. Warner Watkins, M.D., Phoenix, Ariz.

"Surgical Conditions within the Chest, under Roentgen Observations."

William A. Evans, M.D., Detroit, Mich.

"The Radiological Detection of Obscure Foci of Suppuration in the Chest."

Leroy Sante, M.D., St. Louis, Mo.

"Scattered X-rays in Chest Roentgenography."

Rex Wilsey, Physics Dept. Research Lab., Eastman Kodak Co., Rochester, N. Y.

2:00 P.M.—Adjournment

Wednesday 9:00—September 27, 1933.

Section "A"—GASTROINTESTINAL DISEASES

"Duodenitis and Its Roentgenologic Characteristics."

B. R. Kirklin, M.D., Rochester, Minn.

"Application of Roentgenological Findings to the Solution of Gastrointestinal Problems."

Lewis Gregory Cole, M.D., New York City.

"Functional Disturbances of the Colon in Relation to the Roentgen Diagnosis of Organic Colonic Disease."

James T. Case, M.D., Chicago, Ill.

"An Evaluation of a New Procedure in the Study of the Small Intestine."

Eugene P. Pendergrass, M.D., and W. Osler Abbott, M.D., Philadelphia, Pa.

"Statistical Work on Visualization of the Gallbladder by the Oral Method."

R. R. Newell, M.D., San Francisco, Calif.

"Explanation of the Errors in Diagnosis of Gallbladder Disease."

Sherwood Moore, M.D., and Evarts A. Graham, M.D., St. Louis, Mo.

11:00 Recess

"Roentgenology of Duodenal Ulcer: (*a*) The Behavior of The Stomach and Duodenum. (*b*) Methods of Obtaining Outline Deformity in Roentgenograms."

Hollis E. Potter, M.D., Chicago, Ill.

"Roentgenologic Studies of Amoebic Colitis."

J. J. Vallerino, M.D., Panama, R. P.

"An Analysis of 1000 Consecutive Examinations of the Stomach and Duodenum from the Clinical, Roentgenological, and Surgical Viewpoint; with Particular Reference to the Incidence, Diagnosis,

* This program is nearly complete. It combines the scientific programs of the American Radium Society, the American Roentgen Ray Society, the Radiological Society of North America, and the Annual Meeting of the American College of Radiology.

and Treatment of Ulcer and Carcinoma of the Stomach."

Nelson M. Percy, M.D., and David S. Beilin, M.D., Chicago, Ill.

"Dangers of Fluoroscopy and Methods of Protection."

E. T. Leddy, M.D., Rochester, Minn.

"Colon Studies. VII. Variations in the Fixation of the Ceco-Colon: Their Clinical Significance."

John L. Kantor, M.D., and Samuel Schechter, M.D., New York City.

2:00 P.M.—Adjournment

Thursday, 9:00 A.M., September 28, 1933.

Section "A"—DISEASES OF BONES, JOINTS AND BONE TUMORS

"Seventy Cases of Five-Year Cures in Sarcoma of Bone." (Lantern Slides.)

Charles F. Geschickter, M.D., Baltimore, Md.

"Injuries of the Spine, Both Acute and Chronic."

Howard P. Doub, M.D., Detroit, Mich.

"Parathyroid Disease."

Lawrence Reynolds, M.D., and E. R. Witwer, M.D., Detroit, Mich.

"The Treatment of Giant Cell Tumors of Long Bones."

William B. Coley, M.D., and Bradley L. Coley, M.D., New York City.

11:00 Recess

"Osteomalacic Diseases in Monkeys; A Metabolic and Roentgenographic Study."

Ralph S. Bromer, M.D., E. P. Corson-White, M.D., and Irving Stine, M.D., Philadelphia, Pa.

"X-ray Evidences of Necrosis of the Head of the Femur Following Intracapsular Fractures of the Neck."

D. B. Phemister, M.D., Chicago, Ill.

"Infectious Granulomata of the Bones and Joints, with Special Reference to Coccidioidal Disease."

Ray A. Carter, M.D., Los Angeles, Calif.

"Lead Poisoning in Infants and Children."

E. C. Vogt, M.D., and C. F. McKahnn, M.D., Boston, Mass.

Moving Picture—"Reduction of Fractures and Removal of Foreign Bodies under Fluoroscopic Control, Using Oil Immersed Units and Special Fracture Device."

L. G. McCutcheon, M.D., St. Louis, Mo.

"Further Observations on Spontaneous Multiple Symmetrical Fractures."

L. A. Milkman, M.D., Scranton, Pa.

2:00—Adjournment

Friday, 9:00 A.M., September 29, 1933.

Section "A"—UROLOGY AND GYNECOLOGY

"Studies with Opaque Media in Urology."

Leopold Jaches, M.D., and Moses Swick, M.D., New York City.

"Opaque Studies of the Uterus and Pelvis."

Carlos Heuser, M.D., Buenos Aires, Argentina.

"Renal Peristalsis During Pyelonephritis—A Roentgen-Physiologic Study."

Hans A. Jarre, M.D., Detroit, Mich.

"Further Observations in the Diagnosis of Tumors of the Kidney."

Bernard H. Nichols, M.D., Cleveland, Ohio.

11:00 Recess

"The Fate of Thorium Dioxide in the Body after Intravenous Injection."

Ernst A. Pohle, M.D., Madison, Wis.

"Roentgen Examination of the Chests of Five Hundred Newborn with Reference to Pathology Present other than Enlarged Thymus."

Leon Solis-Cohen, M.D., and Samuel Bruck, M.D., Philadelphia, Pa.

2:00 P.M. Adjournment

Saturday, 9:00 A.M., September 30, 1933.

Section "A"—NEUROLOGY and MISCELLANEOUS

"Pituitary Tumors; Radiological Aspects of Diagnosis and Treatment."

Merrill C. Sosman, M.D., Boston, Mass.

"Encephalography."

Karl Kornblum, M.D., and Francis C. Grant, M.D., Philadelphia, Pa.

"Spinal Cord Lesions and Their Recognition by Roentgenologic Methods."

John D. Camp, M.D., Rochester, Minn.

"Visualization of the Cerebrospinal Fluid System, by Air or Oxygen."

A. Howard Pirie, M.D., Montreal, Que.

"Roentgenological Considerations of Sinus Diagnosis with and without Radiopaque Oils."

Edwin C. Ernst, M.D., St. Louis, Mo.

11:00 P.M.—Recess

"The Diagnosis of Accessory Sinuses."

Amedee Granger, M.D., New Orleans, La.

"Diagnosis of Mastoid Disease."

Frederick M. Law, M.D., New York City.

2:00 P.M.—Adjournment

"The Genealogy of the X-ray."

A. W. Crane, M.D., Kalamazoo, Mich.

Title to be given later.

Seeley G. Mudd, M.D., Pasadena, Calif.

"Some Practical Application of the Recent Advances in Physics."

W. D. Coolidge, Ph.D., and E. E. Charlton, Ph.D., Schenectady, N. Y.

"The Solution of some Problems in High Voltage Equipment."

Chas. C. Lauritsen, Ph.D., Pasadena, Calif.

"Application of Physical Measurements in Clinical Irradiation."

Lauriston S. Taylor, Washington, D. C.

"Physical and Biological Characteristics of 700 kv. X-rays."
G. Failla, D.Sc., New York City.
"Distribution of X-rays within the Human Body."
E. H. Quimby, M.A., and M. M. Copeland, M.D., New York City.
"The Measurement of Gamma Rays in Roentgens."
G. Failla, D.Sc., and L. Marinelli, B.Sc., New York City.
"Heublein's Method of Continuous Irradiation of the Entire Body in the Treatment of Generalized Neoplasms."
Floyd F. Craver, M.D., and William S. MacComb, M.D., New York City.
"The Problems of Protection and their Solution in Short Wave Therapy."
T. Leucutia, M.D., Detroit, Mich.
"The Place of Roentgenology in the University: A Program of Teaching and Investigation."
Paul C. Hodges, M.D., Chicago, Ill.
"Studies on Composite X-ray Filters."
A. Mutscheller, Ph.D., Westinghouse X-ray Corp., Long Island City, N. Y.

2:00 P.M.—Adjournment

Wednesday, 9:00 A.M., September 27, 1933.

Section "B"—BREAST DISEASES

"Further Observations in Roentgen Diagnosis of the Breast."
Ira H. Lockwood, M.D., Kansas City, Mo.
"Combined Surface and Interstitial Radiation in the Treatment of Mammary Cancer."
Albert Soiland, M.D., Los Angeles, Calif.
"Irradiation Results in the Treatment of Cancer of the Breast."
Burton J. Lee, M.D., New York City.
"Distribution of X-ray Intensity in Tissue with the Central Ray Striking the Surface, at Angles other than 90 Degrees."
Ernst A. May, M.D., Newark, N. J.

11:00—Recess

"Technique and Results of Irradiation in Carcinoma of the Breast."
George E. Pfahler, M.D., and Jacob H. Vastine, M.D., Philadelphia, Pa.
"The Treatment of Chest Wall Secondaries in Breast Carcinoma: A Preliminary Report of a New Technique."
Gordon E. Richards, M.D., Toronto, Canada.
"A Classification of Tumors from the Standpoint of Radiosensitiveness."
A. U. Desjardins, M.D., Rochester, Minn.
"Histopathology of Irradiated Hodgkin's Disease and Lymphoblastoma."
Alexander Brunschwig, M.D., Chicago, Ill.

2:00 P.M.—Adjournment

Thursday, 9:00 A.M., September 28, 1933.

Section "B"—CANCER OF THE MOUTH, SKIN, AND MISCELLANEOUS

"Irradiation Treatment of Cancer of the Lip and Mouth, Technique and Results."
Charles L. Martin, M.D., Dallas, Tex.
"Management of Cancer of the Mouth and the Cervical Lymphatics."
Douglas Quick, M.D., New York City.
"The Treatment of Carcinoma of the Pharynx, Tonsil, and Extrinsic Larynx by Divided Doses of Roentgen Therapy."
Hayes E. Martin, M.D., and Robert E. McNattin, M.D., New York City.
"Cancer of the Skin."
George W. Grier, M.D., Pittsburgh, Pa.
"Results of Irradiation in Diseases of the Skin."
Joseph J. Eller, M.D., New York City.
"Roentgen Therapy of Epitheliomas of the Pharynx and Larynx."
Maurice Lenz, M.D., Cornelius Coakley, M.D., and Pardy Stout, M.D., New York City.

11:00—Recess

"The General and Medical History of Electricity Told with Old Books Taken from my Library."
Leo E. Pariseau, M.D., Montreal, Que.
"Three Years of 300 kv. Cancer Therapy."
J. Ernest Gendreau, M.D., Montreal, Que.
"Protracted Irradiation in the Treatment of Neoplasms of the Mouth and Pharynx: A Comparison between X-rays (Coutard Technique), 5 Gram Radium Pack, and Small Radium Pack."
Ira I. Kaplan, M.D., Milton Friedman, M.D., Rieva Rosh, M.D., and Carl B. Braestrup, B.S.C., P.E., New York City.
"The Roentgen-Ray and Radium Treatment of Cancer of the Lip."
Bernard P. Widmann, M.D., Philadelphia, Pa.

2:00 P.M.—Adjournment

Friday, 9:00 A.M., September 29, 1933.

Section "B"—UROLOGY AND GYNECOLOGY, AND ABDOMINAL DISEASE

"Radiation Treatment of Carcinoma of the Bladder."
Benjamin S. Barringer, M.D., New York City.
"Radiation Treatment of Carcinoma of the Cervix."
William P. Healy, M.D., New York City.
"Radiation Treatment of Carcinoma of the Uterus."
Henry L. Schmitz, M.D., Chicago, Ill.
"Benign Diseases of the Uterus."
Leda J. Stacy, M.D., Rochester, Minn.
"Studies in the Diagnosis and Treatment of Teratoma Testis."
Russell H. Ferguson, M.D., New York City.

11:00—Recess

"The Multi-perforated Lead Screen in Deep Therapy."
F. Liberson, M.D., Stapleton, N. Y.
"Radium Treatment of Primary Carcinoma of the Rectum."
H. H. Bowing, M.D., Rochester, Minn.
"Abdominal Hodgkin's Disease."
Edward L. Jenkinson, M.D., and A. R. Elliott, M.D., Chicago, Ill.
"Radiology and the Radiologist."
Edward H. Skinner, M.D., Kansas City, Mo.
"Technique of Treatment of Cancer of the Cervix with Radon."
Frank E. Simpson, M.D., Chicago, Ill.

2:00 P.M.—Adjournment

Saturday, 9:00 A.M., September 30, 1933.
Section "B"—MISCELLANEOUS

"Visualized Lymphatics."
Leon J. Menville, M.D., New Orleans, La.
"Pernicious Leucopenia."
Wm. Edward Chamberlain, M.D., Philadelphia, Pa.
"Diagnosis and Treatment of Parathyroid Dysfunction."
Edwin A. Merritt, M.D., and Edgar M. McPeak, M.D., Washington, D. C.
"Radium in the Treatment of Hyperthyroidism."
Roland E. Loucks, M.D., Detroit, Mich.
"Roentgen Treatment of Hyperthyroidism."
Thomas A. Groover, M.D., and A. C. Christie, M.D., Washington, D. C.

11:00—Recess

"The Malignant Diseases of the Thyroid Gland."
U. V. Portmann, M.D., Cleveland, Ohio.
"A Report of 62 Cases of Herpes Zoster Treated with X-rays."
John M. Keichline, M.D., Huntington, Pa.
"Primary New Growths Involving the Hand."
Bernard F. Schreiner, M.D., and William H. Wehr, M.D., Buffalo, N. Y.
"Training for Radium Therapy."
William H. Cameron, M.D., New York City.
Title to be given later.
Pedro L. Farinas, M.D., Havana, Cuba.

2:00 P.M.—Adjournment

PENNSYLVANIA RADIOLOGICAL SOCIETY

The annual meeting of the Pennsylvania Radiological Society will be held at the Penn-Alto Hotel, Altoona, Pa., on May 24 and 25, 1933. The Meeting begins at 1:15 p.m. on Wednesday, May 24.

DAVID ANDERSON-BERRY PRIZE

A David Anderson-Berry Gold Medal, together with a sum of money amounting to about £100, will be awarded in July, 1935, by the Royal Society of Edinburgh to the person, who, in the opinion of the Council, has recently produced the best work on the nature of roentgen rays in their therapeutic effect on human diseases. A further notice will be published early in 1935. A similar award will be made every three years.

BOOK REVIEWS

Books Received Are Acknowledged under Heading: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

PAPERS RELATING TO THE PITUITARY BODY, HYPOTHALAMUS AND PARASYMPATHETIC NERVOUS SYSTEM. By Harvey Cushing, Professor of Surgery (Emeritus), Harvard University and recently Surgeon-in-Chief, Peter Bent Brigham Hospital, Boston. Cloth. Price, $5.00. Pp. 234, with 99 illustrations Springfield, Illinois; Baltimore, Maryland: Charles C Thomas, 1932.

Cushing has again demonstrated the remarkable results of his unfailing zeal for the acquisition of new knowledge regarding the functions and mechanisms of the central nervous system. In this new work he gives us an insight into the complexities of the diencephalon and the anatomically and physiologically closely related pituitary body. "Here in this well-concealed spot, almost to be covered by a thumbnail, lies the very mainspring of primitive existence—vegetative, emotional, reproductive—on which, with more or less success, man has come to superimpose a cortex of inhibitions."

Thanks to Cushing's efforts in individual experimentation and in correlating the numerous and widely scattered works of others, the "disturbances of this ancestral apparatus are beginning to stand out in their true significance."

No review of this group of closely related papers can possibly convey a tithe of the immense amount of clinical and experimental observations contained in them, so completely filled is every page with a digest of correlated facts and speculative interpretations. Suffice it to say that here will be found the sum of our present knowledge of the functions of the posterior lobe of the hypophysis, and of the surprising interrelationship between it, the tuber cinereum and the nuclei in the walls of the third ventricle. Under localization of function in the interbrain are discussed diabetes insipidus, adiposity, carbohydrate metabolism, a possible thermoregulatory center, and pathological sleep.

Especially interesting are the results of the intraventricular injections of pituitrin, since they clearly indicate a parasympathetic center in the walls of the third ventricle and suggest that this division of the autonomic nervous system is equally as important as the thoracolumbar (commonly called sympathetic) system. This work on the intraventricular administration of various organ extracts and drugs opens up an entirely new field in pharmacological and physiological investigation.

A thorough exposition of the basophil adenomas of the pituitary body and their clinical manifestations constitutes the third division of this new book. The basophilic syndrome has only recently been recognized, largely through Cushing's work, and the disease will probably prove to be much more common than the few proved examples now indicate. This condition should be of special interest to the roentgenologist since the approved method of treatment apparently will be roentgen therapy.

The final chapter deals speculatively with the conception which is steadily gaining ground of the neurogenic origin of peptic ulcer. Further evidence in support of this hypothesis is furnished by some of Cushing's cases.

I can recommend this book as a wonderful fund of clinical and experimental observations and clear cut deductions on the functions and abnormalities of function of the pituitary gland, the infundibulum and the third ventricle. It is a book to be read from the beginning and every part deserves careful study.

MAX MINOR PEET

CLASSIC DESCRIPTIONS OF DISEASE: WITH BIOGRAPHICAL SKETCHES OF THE AUTHORS. By Ralph H. Major, Professor of Medicine, University of Kansas School of Medicine. Cloth. Introductory price, $4.50. Pp. 630, with 130 illustrations. Springfield, Illinois; Baltimore, Maryland: Charles C Thomas, 1932.

A book such as the one produced by this author has long been awaited by the medical profession but especially by teachers of medicine. To Sir William Osler must be given major portion of the credit for emphasizing successfully the value of the historic background in the training of physicians, and it is entirely possible that the author of this volume owes

his initial inspiration for this endeavor to this master of medicine.

To the reviewer it has always appeared regrettable that a student or physician could speak glibly of a "Corrigan pulse," the "Stokes-Adams syndrome" or "Kussmaul's breathing" without the slightest idea or curiosity concerning the individual's name which was associated with the condition. And yet, this is usually the situation. Medical educators have long thought that some acquaintance with the historical aspects of our profession is desirable and yet the addition of a systematic course in this subject to the curriculum usually fails to stimulate the desired interest. There may be several explanations of this which need not be discussed here, but certainly the fact that many students have an inadequate conception of general history is one important reason why the systematic teaching of historical medicine usually falls on barren soil. Dr. Major's book affords a more logical and refreshing approach, for, as he says "When, in a clinic, Corrigan's description of the pulse in aortic insufficiency is read while a patient suffering from this disease is presented, the pulse is no longer a mere name, but becomes endowed with a definite personality." To interest one in the life and accomplishments of an individual is the natural and logical method of stimulating a desire for knowledge of the contemporary history of the period in which he lived.

The busy practitioner might in these trying times secure a well-deserved respite from his cares if he used only a few minutes at the end of a busy day to read the appropriate articles bearing upon any disease condition which had recently been observed. Even an occasional reference might lay the foundations for a gratifying avocation which might prove eventually an excellent source of interest and diversion.

The author has used excellent judgment in assembling his material, for he has selected "either the first known, one of the earliest, or one of the most interesting accounts of the disease in question." Not infrequently the earliest description is not the classic delineation of a disease, but may consist only of a few brief sentences which barely indicate that the author had dimly recognized the syndrome. For example, Paracelsus did apparently sense that cretinism might have a significant association with endemic goiter because he mentioned that some foolish men had goiters. For the most excellent description, however, of thyroid insufficiency we are indebted to Sir William Gull who published his paper "On a Cretinoid State Supervening in Adult Life in Women" in 1873, in which he presented a complete and unmistakable clinical picture of the disease. One wonders, however, concerning that great group of competent but historically unknown clinicians who might have sown the seeds, either directly or indirectly, in the minds of the recognized medical contributors which caused them to present "new" syndromes to the medical world. Or still more regrettable is the loss, for the present, of possibly even more vivid descriptions of disease that now repose in obscure and forgotten medical publications awaiting the day when they will receive their delayed but well-deserved recognition.

The volume contains 241 contributions which are presented in their entirety or in part, and 130 illustrations. In addition, many brief but well written biographical sketches are included which add greatly to the value of the book. To regard this volume as a mere compilation of epoch-making medical articles does the author a great injustice for the finished work indicates a fine sense of judgment, a scholarly knowledge of medical history, and an ability to cope with various languages, including the intricacies of medieval Latin.

It is interesting to note that the writings of a number of contemporary clinicians and scientists have appropriately been included. Surely the contributions of Frederick Banting, George R. Minot, James B. Herrick, and a number of other modern observers, easily qualify as "classic descriptions of disease." The author recognized the importance of Dr. Herrick's contributions by including two of his most important articles, both of which are of great permanent value. It is stated in the biographical sketch of this author that "His outstanding contributions are his original description of sickle cell anemia and his classic work on coronary occlusion. While this latter condition had been noted before the appearance of Herrick's paper, his masterful studies have cleared up the confusion surrounding this disease and have sharply delineated this most important syndrome." His paper dealing with sickle cell anemia deserves to be preserved, first because it is the original clinical description of this disease which was so complete that very little of importance has been added in the intervening

twenty-three years, and second, because it is a model for case reports, characterized by brevity, conciseness and careful, descriptive, scientific writing.

It is inevitable that some readers will experience a certain amount of regret because subjects in which they have a great personal interest have been omitted or sparsely represented. To heed all of the suggestions of intense and enthusiastic readers concerning additional articles which should be included would be impossible. The reviewer presents for serious consideration, nevertheless, William Withering's "An Account of the Foxglove and Some of its Medical Uses: with Practical Remarks of Dropsy and other Disease." This remarkable therapeutic classic should be made easily accessible to all as it deserves to be read again and again by every medical student and practitioner of medicine.

The author and publisher are to be congratulated upon the production of such a volume and it is warmly commended to medical students and the profession in general.

Cyrus C. Sturgis

Otologische Röntgendiagnostik. Von Dr. Ernst G. Mayer, Privadozent für Röntgenologie, Assistent am zentral-röntgeninstitut, Professor G. Holzknecht, Wien. Klinischer Beitrag: Die Wertung und Verwendung der Röntgenbefunde in der Otologie. Von Dr. Karl Eisinger, Assistant und röntgenologischer Referent der Univ.- Klinik für Ohren-, Nasen- und Kehlkopfkrankheiten, Professor Dr. H. Neumann, Wien. Paper, price RM 75; bound, price RM 78.60. Pp. 357, with 611 illustrations and 6 tables. Wien: Julius Springer, 1930.

That Ernst Mayer, pupil and assistant of the great Holzknecht, has made excellent use of the large amount of material in the clinics of Neumann and Hajek is evidenced by his work on "Roentgenological Diagnosis in Otology." It is exceedingly well planned, comprehensive, devoid of superfluous detail, and the subject matter is so graphically presented that it may serve as a text even to those with only a limited knowledge of the German language. In short, it maintains the high standard of all the works that have so far emanated from the Holtznecht School.

The author begins with a short history of the development of this special branch of diagnosis. He then discusses in chronological order the various projections of the mastoid which have been recommended, beginning with Henle, 1904, Schüller, 1905, Lang, 1909, down to the present time, each projection being illustrated by clear diagrams. Then a chapter on Normal Roentgen Anatomy, followed by one on variations and their influence in diagnosis. This is followed by an extensive and very well illustrated section on Pathological Anatomy. He first considers inflammation, acute and chronic, followed by specific inflammations, i.e. tuberculosis and lues. Next, tumors, benign and malignant, with a discussion of the differential diagnosis between tumors and changes produced by infection. Under tumors he considers carcinoma, sarcoma, endothelioma, chloroma and myeloma, also the influence of tumors of the cerebellopontine angle.

There is a short section on fractures, foreign bodies and their localization, operation defects and abnormalities of development. This is followed by rare and unusual conditions, such as osteopsathyrosis idiopathica, Paget's disease, Ménière's disease, otosclerosis, hydrocephalus and craniostenosis, finally diseases of the ear muscles.

The book is concluded by a very well written section on the clinical value and significance of roentgen findings in otology by Eisinger of Vienna, in which he discusses inflammatory conditions, indications and contraindications for operation, errors in roentgen diagnosis, the value of roentgen investigation in postoperative complications, the diagnostic value of the findings in tumors and rare conditions.

One of the most valuable features of the work to the roentgenologist is the carefully executed drawings accompanying the illustrations, with every important anatomical line clearly indicated by letters with explanatory legend below.

Those with a very limited knowledge of German will be able in a short time, with the aid of a dictionary, to understand the drawings.

Another exceedingly useful feature in the chapter on Roentgen Anatomy is a series of unanimated drawings, beginning with one line illustrating a point in anatomy then gradually adding lines until there is a complete picture containing every anatomical land mark revealed by the projection. Mayer has here applied a well-known principle in pedagogics, treating anatomy in a geographical manner similar to map drawing. The reader with a little

practice with pencil by means of the illustrations in a short time can gain a thorough knowledge of the roentgen anatomy revealed by each of the standard projections of the mastoid region. Mayer uses this method to teach the errors of interpretation which might result from incorrect projection of the different standard positions.

Roentgenology and otology are greatly indebted to Ernst Mayer for the painstaking treatment of a difficult subject in medical diagnosis. The publishers are to be congratulated upon the excellence of printing and paper. The illustrations are without question the best I have ever seen and in fact are remarkable when the difficulties of reproducing roentgenograms of bone pathology are considered. The book is, in my opinion, by far the best presentation of the subject in roentgen literature today. The illustrations alone are worth the cost of the book.

W. C. Wescott

Radiologic Maxims. By Harold Swanberg, B.Sc., M.D., F.A.C.P., Editor, The Radiological Review; Radiologist, Saint Mary's Hospital and Blessing Hospital, Quincy, Illinois, etc. With a Foreword by Henry Schmitz, A.M, M.D., LL.D. Professor of Gynecology and Head of the Department, Loyola University School of Medicine. Cloth. Price $1.50. Pp. 127. Quincy, Illinois, Radiological Review Publishing Company, 1932.

This is a very interesting, readable little book, full of helpful hints for the harassed diagnostician and therapist whose mind turns to roentgen rays or radium as a possible source of aid. Well-known authorities are quoted freely. The text, made up of passages selected from the writings of various well-established clinicians, is presented in the form of selected paragraphs, sometimes as long as a page, grouped in such a manner as to render reference easy.

James T. Case

Vol. XXIX, No. 4

DEPARTMENT OF TECHNIQUE

Department Editor: Robert B. Taft, 105 Rutledge Ave., Charleston, S. C.

A SIMPLIFIED TECHNIQUE FOR ROENTGENOGRAPHIC EXAMINATION OF THE OPTIC CANALS

By JOHN D. CAMP, M.D.
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and
CESARE GIANTURCO, M.D.
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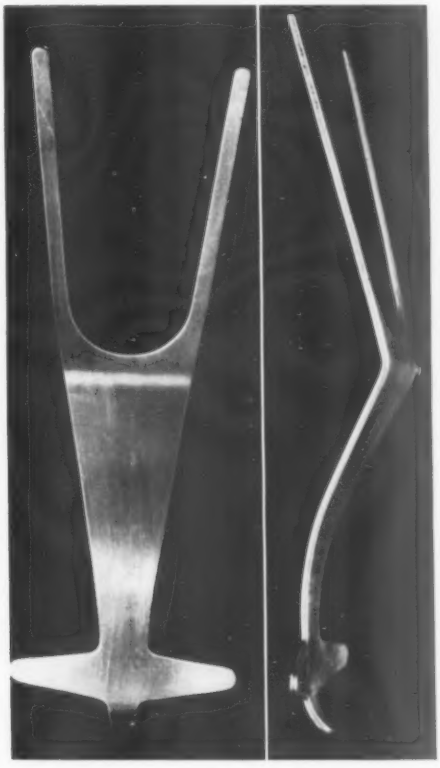
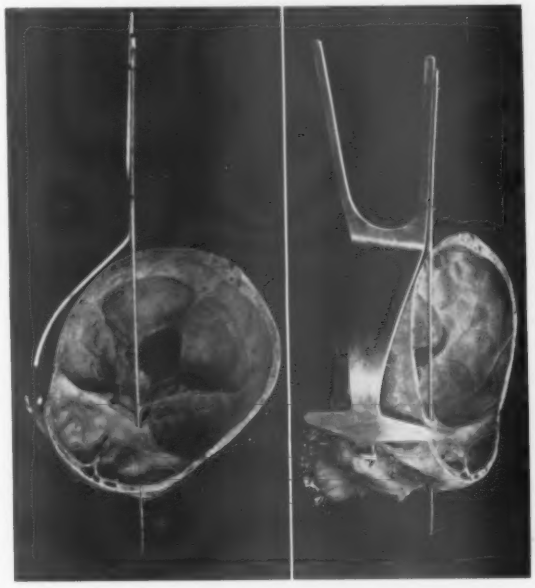
ROCHESTER, MINNESOTA

THE technique and the localizer described below are the result of an attempt to devise a simple, practical, and accurate method for making roentgenograms of the optic canals. In perfecting this technique it was our purpose to eliminate the necessity for measuring certain angles or using special head rests at each examination. The localizer which we have devised is based on the existence of certain fixed and readily distinguishable anatomic landmarks (the external angle of the orbit, the squama temporalis, and the superior attachment of the concha of the ear) and their relation to a point on each side of the skull through which the axis of the optic canal, if extended, would pass. This point, in the average skull, is so constant in situation that by correlating it with the pre-



a *b*

Fig. 1. Duralumin optic canal localizer.



a *b*

Fig. 2. Optic canal localizer in position on dried skull. The superior prong of the instrument coincides with line of direction of optic canal (demonstrated by wire).

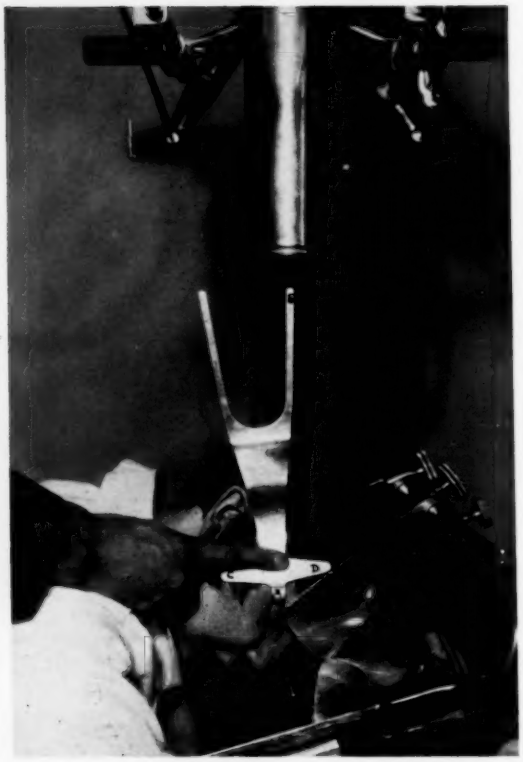


Fig. 3. Lateral view of patient's head properly centered by means of localizer for examination of left optic canal. Points *A*, *B*, *C*, *D*, *E*, are explained in text.

viously mentioned landmarks, a device for representing the prolongation of the line of axis of the optic canal can readily be made. Such a device, made of duralumin, is represented in Figure 1, and the anatomic basis for its use is represented in Figure 2, *a* and *b*.

The technique for the use of this localizer is as follows: The center of one half of the film is first placed beneath the center of the cone on the roentgenographic tube stand and the other half of the film is covered with a suitable lead mask. The patient is now placed prone on the table with one orbit at the center of that part of the film which is directly under the cone. Point *A* of the localizer is placed at the external angle of the opposite orbit, and the lower edge *B* of the instrument is placed against the superior attachment of the concha of the ear (Figs. 3 and 4). The wings (*C* and *D*) of the localizer, because of their length, will rest against the tissues over the squamous portion of the temporal bone and stabilize the instrument. The head of the patient is now manipulated until the superior prong, *E*, of the localizer coincides with the path of the central ray. When the patient's head is properly placed the central ray will enter the skull at a point directly over and in line with the optic canal as shown in Figure 2, *a*. The instrument is now removed, the head immobilized, and the exposure made. The exposed half of the film is now covered with lead and the above procedure repeated for the demonstration of the opposite optic canal and orbit on the unexposed half of the film. When the patient is properly posed the resulting roentgenogram compares with that shown in Figure 5, in which the shadows of the optic canals are indicated by arrows.

Fig. 4. Vertical view of patient's head properly centered by means of localizer for examination of left optic canal.

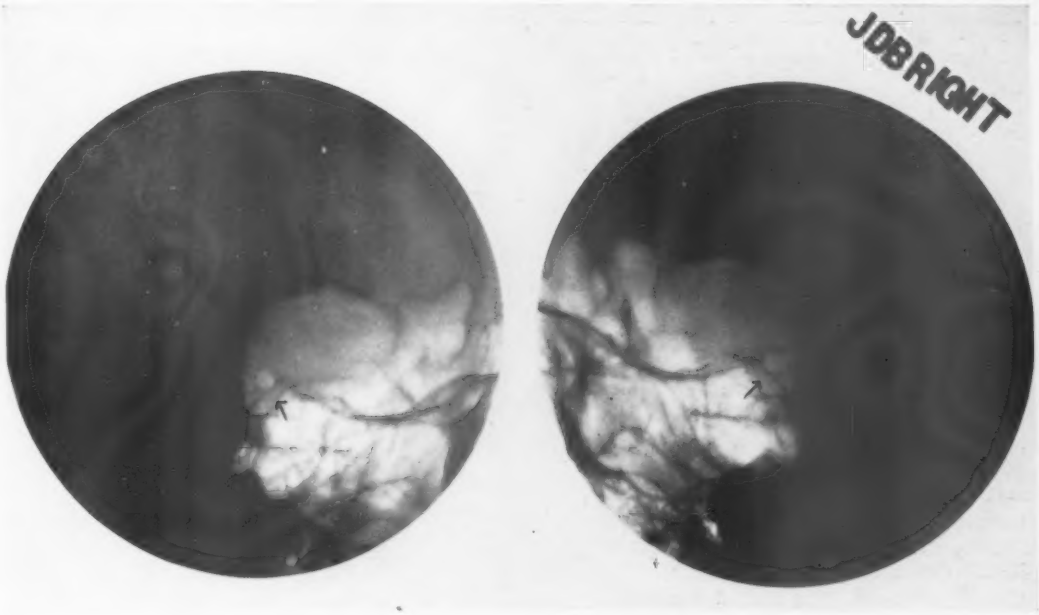


Fig. 5. Roentgenogram of right and left optic canals obtained by use of localizer. Shadows of canals indicated by arrow.

Figures 3 and 4 show the examination being made with the patient's head resting on a 23° angle-board, such as is commonly used for roentgenography of the sinuses. An angle-board makes the position somewhat more comfortable for the patient but is not absolutely necessary, since the localizer will automatically center the optic canal regardless of the angle of inclination of the head.

The simplicity of this technique is obvious, and its practicability is demonstrated by the fact that it has been used by many inexperienced technicians with uniformly satisfactory results. The value of such a procedure in accurately reproducing roentgenograms of the same structure at subsequent intervals for comparative purposes is apparent. In our examination we use, as a routine, a film-target distance of 30 inches (76 cm.). At that distance the average diameters of shadows of normal canals coincide with the averages given by Goalwin and White.

It should be mentioned that the technique is applicable to the skull of usual shape. In unusually long or small round heads there is a slight variation in the point of emergence of the axis of the optic canals. This variation is automatically compensated for in such cases if the head is posed so that the prong *E* of the localizer is parallel to the central ray but not exactly coincident with it.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

HEAD

Kennedy, Foster, and Wortis, S. B. How to treat head injuries and appraise them. *J. Am. M. Ass.*, April 16, 1932, *98*, 1352–1353.

Of 1000 cases of acute head injury which showed positive skull fracture or brain laceration, the mortality was 37.8 per cent. Roentgenograms were made in 499 of these cases, of which 230 were negative, 186 revealed linear fracture of the vault, 20 depressed fractures of the vault, and 63 fractures of the base. Lumbar puncture showed 801 of 846 cases to have bloody spinal fluid. Of 257 autopsies only 14 showed meningitis, and 2 brain abscess. Bleeding from the nose, mouth or orbital tissues occurred in 701 cases. The majority of the cases showed evidence of neural damage.

Treatment should include lumbar puncture, dextrose by intravenous and rectal routes, elevation of the head of the bed, and caffeine sodiobenzoate. Decompression, debridement, and antimeningococcus serum, may be indicated.

A small minority of patients with head injuries, including skull fractures, return later with complaints. If the degree of injury, symptoms immediately following the accident, and the physical and neurologic reaction, do not harmonize suggestion neurosis should be suspected. These cases are best handled by prompt accurate diagnosis and treatment, speedy adjudication, and economic adjustment by a single settlement. The cases should then be closed beyond the possibility of being reopened.—*E. W. Hall.*

Arnell, Sigfrid. Encephalography with solution of contrast salt. *Acta radiol.*, 1932, *13*, 43–50.

The author made roentgen examinations of the skulls of corpses after having filled the subarachnoid spaces by suboccipital puncture with a contrast solution. He used aqueous solutions of 20 per cent abrodil, 20 per cent lithium iodide and 25 per cent potassium iodide and tordiol mixed with 2 parts of water. These solutions all have a greater specific gravity than the spinal fluid and so flow to the lowest part of the spaces into which they are injected. The anatomy of the subarachnoid spaces is described. It is very easy to obtain a contrast filling of the subarachnoid spaces in the side of the skull that is turned downward. As a rule 15 to 20 c.c. of the fluid is sufficient. Spinal fluid is withdrawn before it is injected. Stereoscopic films are taken in several directions after the injections. The author is now trying to find a substance that can be used in living subjects. —*Audrey G. Morgan.*

NECK AND CHEST

Pyrah, L. N., and Allison, P. R. Some sialograms. *Brit. M. J.*, Dec. 5, 1931, *2*, 1028–1030.

Lipiodol is injected by means of a rectal syringe to which is screwed a modified lacrymal duct needle. This needle has a bulbous end which prevents trauma. Introduction of the needle causes a slight cutting pain not objectionable to the patient. The needle is inserted about 1 inch, 0.5 to 1 c.c. of lipiodol is sufficient. A sensation of discomfort in the gland increases as the finer ducts are filled. The procedure is the same for submaxillary and parotid glands. The parotid is roentgenographed in the lateral position, the head hyperextended to open the space between the jaw and the vertebral column. The submaxillary gland is roentgenographed in the lateral position with the tongue pressed to the roof of the mouth.

Sialography is used: In chronic parotitis with subacute exacerbations in which it reveals that one essential feature of the pathology of the disease—dilatation of the ducts and alveoli. By means of sialography, a tumor in the region of the gland may be differentiated as to whether it is derived from the gland or from adjoining structures. Injection of lipiodol may be of use in the localization of calculi. The position and track of salivary fistulae may be thus traced. Four cases in which the procedure was used are reported in detail.—*E. I. L. Cilley.*

Barclay, A. E. The origin of the Zenker pouch of the pharynx. *Acta radiol.*, 1932, *13*, 87–89.

This is a letter from Barclay in which he discusses Laurell's work on this subject and disagrees with Laurell's theory that these pouches

are caused by pulsion. He thinks the pouches are caused by adhesions to the vertebrae which bring about traction. The lifting of the laryngopharynx would naturally drag on the posterior pharyngeal wall if it were adherent and lead to the formation of a pouch which would increase in size merely from repeated filling with food. There is a weak triangular spot on the posterior wall of the pharynx where there are only circular muscle fibers and traction here is very apt to result in a pouch.

As adhesions indicate old injury or disease Barclay decided to look for evidences of pathological changes in the spine in the only case of Zenker's pouch that he had available. Two roentgenograms of the case are reproduced which show a localized spondylitis between two vertebrae just behind the site where such a pouch would originate. This supports his hypothesis that these pouches are caused by traction independently of increased or decreased pharyngeal pressure.—*Audrey G. Morgan.*

Paschetta, Vincent. Étude radiologique de la glande mammaire. (Roentgen study of the mammary gland.) *Bull. et mém. Soc. de radiol. méd. de France*, July, 1931, *19*, 346–348.

The roentgen examination of the mammary gland is little used. The author was able to find only one recent article, that of Warren (published in the *Am. J. Roentgenol. & Rad. Therapy*, 1930, *24*, 113–124), dealing with the subject.

The technique of examination consists in placing the patient in a lateral position (left side for left breast and right side for right breast) with the arms above the head, the breast resting in the center of the film. A soft tissue exposure is used. (1) *Normal.* The roentgenogram of the normal breast shows the nipple and five to eight fine slightly opaque bands corresponding to the galactophore ducts. The pectoralis is well outlined and the fascia of the ribs is clearly visible. (2) *Mammitis.* In chronic mammitis the normal image is somewhat accentuated, the galactophore ducts appearing thicker and somewhat more opaque; the sclerosed gland forms a visible opaque mass with more or less well-defined borders. Less frequently there is a "nebulous" image. Two facts are of diagnostic importance: (*a*) the phenomena are bilateral, and (*b*) the pectoralis major is plainly visible. (3) *Cancer.* (*a*) In the beginning stage the neoplastic mass is distinct, showing unsharp borders and a tendency to extension towards the axilla; (*b*) in the more advanced stage the cancer invades the pectoralis major as well as the skin, retracts the nipple and extends towards the axilla. Often the entire mammary gland is replaced by an opaque irregular mass with unsharp borders and striations into the normal tissues not unlike those observed in osteosarcoma. These striations, however, are not pathognomonic, as claimed by Warren, since they are observed also in subacute mammitis. The important feature in all cancers is the unilaterality of the lesion. (4) *Abscess.* This leads to a rounded shadow, the size of which varies from a cherry to a walnut, or even larger, and which plainly appears within the structures of the gland. The opposite side as a rule is normal or shows signs of a subacute mammitis. (5) *Pregnancy.* (*a*) During the ninth month there is a congestion of the entire gland (resembling the picture of mammitis) with good outline of the pectoralis major, the galactophore canals being dilated, voluminous, distinctly visible; (*b*) during the fourth month the gland is only moderately congested but the ducts appear plainly. The picture is not unlike that of chronic mammitis. A check-up examination one month later reveals an increase of the shadows in case of pregnancy, this being of differential diagnostic importance; (*c*) during puerperium the symptoms are in regression although the images of the ducts appear plainer.

The conclusion is reached that roentgenography of the breast represents a certain interest inasmuch as it furnishes an additional method of examination in affections with un certain diagnosis.—*T. Leucutia.*

Holzmann, Max. Aneurysma dissecans der Brustaorta im Rontgenbild. (Roentgen picture of dissecting aneurysm of the thoracic aorta.) *Acta. radiol.*, 1932, *13*, 21–34.

The roentgen findings in 2 cases of dissecting aneurysm of the thoracic aorta are described and illustrated. The diagnosis was confirmed in both cases by autopsy. In the ventral projection the roentgen findings are characteristic only in cases in which the aneurysm springs from the convexity of the aortic arch or else from the side wall of the aorta. The shadow of the aorta is widened and the aneurysm is seen inside it as a lighter shadow of moderate width surrounding the denser central shadow formed by the bulb of the aorta. In chronic dissecting aneurysm there is no marked bulging of the wall. If there are such dilatations it indicates secondary aneurysmal changes in the outer wall

which may also occur in acute cases. In the descending aorta dissecting aneurysm is much less clearly demarcated and sometimes cannot even be seen. It is questionable whether irregularities in the outline of these aneurysms have any diagnostic significance.—*Audrey G. Morgan.*

Köhler, Bjorn. Eine missglückte Bronchographie. (An unsuccessful bronchography.) *Acta radiol.*, 1932, *13*, 54–56.

A boy of nine came for examination on account of physical signs at the left base. A lipiodol injection was given by the usual technique but no contrast material was seen in the lungs. A second and a third injection were given. Still no contrast medium was seen in the lungs but there was a strip of contrast bounded on one side by the superficial and median fascia of the neck and on the other by the deep fascia. No explanation of this distribution of the contrast medium is given.—*Audrey G. Morgan.*

Jäderholm, K. Bruno. Ein Fall von bullösem Emphysem. (A case of bullous emphysema.) *Acta radiol.*, 1932, *13*, 51–52.

A case is described in a boy of eighteen who had had pneumonia three times, the last time at the age of eight. He became sick July 2, 1931, with symptoms of acute infection and slight dyspnea. On admission to the hospital a few days later he had no subjective respiratory symptoms but the physical findings indicated pneumothorax of the left lower lobe. Bronchography with lipiodol, however, showed an absolutely normal bronchial tree. There were no dilatations or stenoses of the bronchi and no changes in the hilus shadow or elsewhere in the lung fields. There was no explanation therefore of the increased air content of the left lower lobe except a bullous emphysema, probably as a result of the pneumonias in childhood. There was no change in the chief bronchus that could have caused a valve effect.—*Audrey G. Morgan.*

Dunham, Ethel C. Atelectasis in the newborn. *Am. J. Dis. Child.*, March, 1932, *43*, 594–603.

Dunham reports 6 cases of atelectasis in the new-born. Roentgenograms were taken in all of these cases at the time that symptoms or physical signs were present. From a study of these roentgenograms, several points of importance in making a diagnosis of atelectasis are emphasized. The lung fields may show a general haziness, and the observer may regard this appearance as due to poor technique in taking the films when it is in reality due to lack of air in the lungs. On the other hand, one or more definite areas of increased density may be seen, or only one lung may show cloudiness of greater or less intensity when the other is clear. When atelectasis involves one lung more than the other a difference in the level of the diaphragm may be evident, the involved side not descending during inspiration as well as the unaffected side. If the area of atelectasis lies in the left paravertebral region, the pulmonary change may not be visible in the films, because it will be obscured by the shadow of the heart.

Dunham defines atelectasis in the new-born as the abnormal persistence of the fetal state of the lungs due to some condition that interferes with the normal functioning of the respiratory center or to mechanical obstruction of the air passages. The chief symptom is cyanosis. Cyanosis caused by atelectasis of the lungs can be differentiated from cynanosis caused by other conditions by means of the roentgenogram. Roentgen examination of the lungs is always indicated when a new-born infant is cyanotic. Administration of carbon dioxide and oxygen was definitely beneficial in several of the cases.—*R. S. Bromer*

Polevski, Jacob. Primary carcinoma of the lungs. *Arch. Int. Med.*, Dec., 1931, *48*, 1126–1137.

The difficulty of diagnosis of carcinoma of the lungs for the general practitioner has caused the author to attempt to establish pathognomonic signs by which this condition may be recognized. This is of importance because the rate of incidence of the disease is on the increase, which increase is actual and not merely due to the greater frequency in the diagnosis. There is a symptom-complex consisting of a peculiarly characteristic history and definite physical signs by which the average practitioner, in a large majority of cases, should arrive at a correct diagnosis.

The characteristic history consists of a patient of the cancer age, strikingly free of previous pulmonary complaints, who is more or less suddenly taken with some form of pulmonary disease. This condition continues indefinitely, as so well stated by Professor Erdheim of Vienna, "As the rule is once pneumonia in pulmonary carcinoma always pneumonia for obvious reasons." Pain is the most frequently

elicited complaint, dyspnea, the next, while hemorrhage is not uncommon.

The characteristic physical signs consist of: A high position of the diaphragm on the affected side, paradoxical respiration with a see-saw movement of the diaphragm, pendulum movement of the heart which is drawn over to the side affected during inspiration and away from it during expiration, frequent coalescence of an area of flatness in the infraclavicular area with the substernal area of cardiac dullness.

Six case reports with roentgenograms are given to illustrate the pathogonomonic signs of carcinoma of the lung.

The author's summary is as follows: (1) Primary pulmonary carcinoma can be diagnosed clinically; (2) a characteristic history is obtained in the vast majority of cases; (3) a characteristic complex of physical signs has been described; (4) the fluoroscope is of great aid in doubtful cases and helps to confirm clinically established ones; (5) bronchoscopy and biopsy are rarely necessary to establish a diagnosis.—*Karl Kornblum.*

ABDOMEN

Sturtevant, Mills, and Shapiro, Louis L. Peptic ulcer; association with pulmonary tuberculosis. *Arch. Int. Med.*, Dec., 1931, *48*, 1198–1202.

The association of peptic ulcer with pulmonary tuberculosis has been the subject of much controversy, if one may judge from the references quoted in this article. The sum total of this evidence would indicate that the pathologists have noted the association of ulcer and tuberculosis, while the clinicians, for the most part, have doubted any connection between these two disorders.

The authors in 1926 published a portion of a study of all the peptic ulcers recorded in 7700 necropsy records in Bellevue Hospital. These authors felt that since sufficient evidence has been accumulated to make the coexistence of peptic ulcer and tuberculosis of a possible, if not indeed a probable, frequency beyond what one should reasonably expect even in two disorders so commonly found, it would be worth while to tabulate findings on this association in the 7700 necropsies previously studied and apply the ordinary statistical tests to the figures obtained.

The conclusion arrived at as a result of this study is that there is a definitely increased frequency of peptic ulcer in tuberculosis.—*Karl Kornblum.*

Kasabach, Haig H. Effect of ingestion of water and of dextrose solution on emptying time of normal stomach. *Arch. Int. Med.*, Dec., 1931, *48*, 1237–1240.

This is an investigation of the popular belief that ingested fluid "water-logs" the stomach if taken prior to athletic contests or during exercise. Also, since it is a common practice to give athletes carbohydrates by mouth to supply readily available energy and to avoid hypoglycemia, the purpose of this study was to determine the emptying time of the stomach in healthy young men after the ingestion of water and of dextrose solution during periods of rest and exercise.

The emptying time of the stomach was determined roentgenoscopically in 50 healthy young college students after the ingestion of 500 c.c. of water and of an equal quantity of 50 per cent dextrose solution containing a very small quantity of barium sulphate, with the subjects sitting or walking about, and in 20 cases with the subjects running continuously between observations. No difference was observed in the rate of emptying of dextrose solution and of water in either group. Exercise (running) seemed to produce a definite acceleration in the emptying time of the stomach. In these experiments, as exercise accelerated the emptying of the stomach, it seems justifiable to conclude that dextrose solution in a palatable form could be administered to athletes before a contest in which readily available fuel is required, without fear of producing gastric retention.—*Karl Kornblum.*

Arisz, L. Duodenal ulcer with carcinoma. *Acta radiol.*, 1932, *13*, 41–42.

Two cases are described in which carcinoma developed in callous ulcers of the duodenum. They are considered of interest because carcinomatous degeneration of ulcer of the duodenum is very rare. The first patient was examined for the first time on May 9, 1927 The clinical symptoms were those of ulcer. The bulb was distorted and a niche was found near the pylorus. Internal treatment was effective for a long time but in March, 1930, the patient had to be examined again. The distortion of the bulb had increased. Again ulcer was diagnosed and localized on the bulbar side of the pylorus. A week later resection was performed. The

specimen showed a large callous ulcer but microscopical examination revealed typical carcinoma cells.

The second patient had indefinite symptoms. He was roentgenographed in December, 1924. The bulb showed the typical deformity of ulcer. Under internal treatment the patient remained well until December, 1926, when he had several hemorrhages. Operation was performed and the patient died in June, 1927. Post-mortem examination showed an ulcer near the pylorus which proved on microscopic examination to be carcinomatous.—*Audrey G. Morgan.*

Knutsson, Folke. Die Nischendiagnostik bei sehr grossen Duodenalgeschwüre. (Niche diagnosis in very large duodenal ulcers.) *Acta radiol.*, 1932, *13*, 35–40.

Niches can be demonstrated in a very large percentage of duodenal ulcers—according to Åkerlund in about 75 per cent. Generally the niche is the size of a millet seed to that of a bean and the cases are very rare in which the ulcer is so large that the niche is the size of a walnut. The author describes 4 cases of duodenal ulcer with such giant niches. Just because these large niches are so rare they may be overlooked in the deformed bulb. But on careful examination it should not be hard to differentiate a giant niche from a diverticulum. The niche has a rigid unchangeable form and distally from it the shadow of the bulb is greatly constricted by spastic contraction. The niche cannot be made to disappear by compression. The ulcer can be emptied of contrast material only by change of position and in that case the niche disappears. Sensitiveness on pressure and decreased mobility of the bulb on account of adhesions are further signs of ulcer.

One of the author's cases was that of carcinomatous ulcer which is very rare in the bulb of the duodenum. The others were callous ulcers.—*Audrey G. Morgan.*

Kantor, John L. Common anomalies of duodenum and colon; their practical significance. *J. Am. M. Ass.*, 1931, *97*, 1785–1790.

A series of 3000 private patients with intestinal disorders are studied clinically and roentgenologically with relation to the incidence, symptoms and treatment of certain anomalies. Anomalies are expressions of organic constitutional inferiority and are compensated for and symptomless until the compensatory mechanism breaks down.

Duodenal bands were found in 5 per cent of 1754 roentgenographed patients. They are associated with nausea, headaches, vomiting, vertigo, constipation, and appendicitis. There is a mild or transient obstruction of the duodenum with resultant duodenal irritation of reversed peristalsis. Treatment should correct ptosis and malnutrition. Surgery is indicated when conservative measures fail, and gives good results.

Sixteen per cent of 1614 patients showed redundant colon, with constipation, pain, and gas, as more or less constant symptoms. Relief follows conservative measures, surgery being indicated only in volvulus.

Six per cent of about 1600 patients showed a high cecum and 18 per cent a low cecum. High cecum is of interest only in connection with the appendix. Low cecum is responsible for vomiting, headache, and local pain. Medical management consists in treating the asthentic habitus, neurosis, constipation, and fattening the patient. Surgical treatment should be considered in those rare cases in which no improvement is obtained after careful and prolonged conservative measures.—*E. W. Hall.*

Baer, J. L., Reis, R. A., and Arens, R. A. Appendicitis in pregnancy; with changes in position and axis of the normal appendix in pregnancy. *J. Am. M. Ass.*, April 16, 1932, *98*, 1359–1364.

Previous reports regarding the effect of pregnancy on the position of the appendix are conflicting. The authors studied 78 normal pregnancy cases by barium meals at regular intervals from two months to ten days post partum and found a definite elevation of the appendix, the average displacement being about six fingerbreadths. The cecum and colon are likewise elevated and are compressed.

Pregnancy cannot be considered a predisposing factor in the production of appendicitis but when the appendix has been the seat of infection, as indicated by a history of previous attacks, pregnancy plays a definite rôle in producing symptoms, and the authors' series of 28 cases indicates a marked increase in gangrene and rupture. Incidence is greater in the latter months due to the appendix being lifted from the pelvic to the abdominal cavity in which localization and walling off are less frequent. Abortion is an ever present threat and is more common when drainage is used. Prompt surgical removal of the appendix is indicated regard-

less of the pregnancy. The pregnancy should, however, not be disturbed no matter how severe the appendicitis or how advanced the pregnancy.—*E. W. Hall.*

Renander, Axel. Das Röntgenbild bei Darminvaginationen. (The roentgen picture in intestinal invagination.) *Acta radiol.*, 1932, *13*, 64–79.

A case of ileocolic invagination caused by tumor is described and illustrated with roentgenograms and diagrammatic sketches. The tumor proved on operation to be a lipoma with transition in places to a myxomatous type. The only similar case described in the literature is that of Muff. In his case the tumor was malignant and the invagination extended to the sigmoid while in the author's case the invagination only extended to the transverse colon in front of the flexure. In chronic invagination both contrast enema and contrast meal should be used. The invagination can sometimes be diagnosed in the lumen of the large intestine by the longitudinal contrast stripes running along it. Orally from the head of the invagination, which is formed by the tumor, the haustra are broadened and crowded closely together. Most invaginations in this region are ileocecal rather than ileocolic. In ileocolic invagination the cecum is in its usual place while in ileocecal invagination the shadow of the cecum cannot be seen and the right iliac fossa is filled with loops of small intestine.—*Audrey G. Morgan.*

Pons, A. Pedro, and Sabater, J. M. Vilaseca. Investigaciones sobre la hepatolienografía mediante los preparados de thorio—thorotrast. (Hepatosplenography with thorotrast.) *Rev. med. de Barcelona*, 1932, *17*, 16–34.

Recently it has been found possible to make roentgenograms of the liver and spleen by giving injections of colloidal thorium because the colloid is deposited in the reticulo-endothelial cells of those organs. The authors experimented with this method, using thorotrast which is a 25 per cent colloidal solution of thorium dioxide. They first injected the solution into rabbits, 2 c.c. per kilogram of weight every day for three days, and found it was not toxic. With this dose the spleen showed great density, greater than that of the liver.

The optimum dose for man is 60 to 80 c.c. of the 25 per cent solution given in three daily doses. If there are any signs of intolerance an interval of two or three days may be left between the doses. The injections are given intravenously, being made very slowly. It makes no difference whether they are given before or after meals. The patient should be given adsorbent powders during the days of the test so that intestinal gas may not be mistaken for cysts or tumors. A cleansing enema should be given before the roentgenogram is made. The thorium begins to accumulate within fifteen minutes and within twenty-four hours the contrast is strong enough so that a roentgenogram can be taken, though better roentgenograms are obtained after forty-eight hours or more. The maximum contrast is on the twentieth day, after which the drug begins to be eliminated.

Fourteen cases in which the method was used are described and illustrated with roentgenograms. Good contrast is always obtained with normal livers and spleens. The method is of value in demonstrating the outline, size and form of the viscera and showing pathological conditions, such as cysts, abscesses, and tumors. In diffuse tumor, advanced cirrhosis of the liver and leucemia there may be no contrast. The authors have never seen fever or any of the other by-effects that have been described by some authors but in one case of syphilitic anemia they saw the picture of colloidal shock which was overcome by adrenalin. While thorotrast does not cause hemorrhage in normal subjects it seems to exaggerate any existing tendency to hemorrhage, so that the method should not be used in advanced cirrhosis, active leucemia or any hemorrhagic condition.—*Audrey G. Morgan.*

Phemister, D. B., Rewbridge, Allan G., and Rudisill, Hillyer. Cholecystitis and cystic duct obstruction. *J. Am. M. Ass.*, Dec. 19, 1931, *97*, 1843–1847.

Large gallstones containing a large percentage of calcium carbonate have been rarely reported. In 7 cases of this condition there was found obstruction of the cystic duct by a cholesterol stone, the calcium deposits being apparently secondary to the obstruction. The calcium is found either as large stones or as a milk-like bile due to precipitated white flakes. The density of the "milk bile" may be so great as to resemble a well-filled gallbladder following administration of material for gallbladder visualization. In cases reported there was calcification of the wall of the gallbladder and of the cystic duct at the point of impaction.—*E. W. Hall.*

Crandall, Lathan A., Jr. Mechanisms of the contraction and evacuation of the gallbladder. *Arch. Int. Med.*, Dec., 1931, *48*, 1217–1224.

The purpose of the study that forms the basis of this paper is the determination of what mechanisms are responsible for the relatively complete emptying that indubitably occurs following a mixed meal. A brief reference is made to some of the theories advanced in regard to this subject. Since much of the evidence is contradictory, the author has, by further experimental work, attempted to check on some of the mechanisms advanced for emptying of the gallbladder.

The effect of reflex and direct stimulation of the extrinsic nerves was investigated. Sham feedings and direct stimulation of the vagus and splanchnic nerve in dogs, and psychic stimuli and the injection of epinephrine in human beings, were not found to have any effect on the motility of the gallbladder. Since sham feeding in the dog and psychic stimuli in man do not affect the shadow of the gallbladder, it is probably not necesary for the patient who has been given the Graham test to avoid the sight or smell of food.

Experiments were performed to investigate the spontaneous emptying of the gallbladder which Graham and his associates have ascribed to a washing out of the bile in the gallbladder by freshly secreted bile from the liver. In these experiments it was found that the viscosity of the opaque oils used for experimental purposes is of considerable importance in attempting to determine the ability of the gallbladder to empty spontaneously. The gallbladders of dogs, when filled with brominized oil which is less than three times as viscous as bile, empty about one-half of the oil spontaneously in from eighteen to twenty-four hours. The gallbladders of dogs when filled with iodized oil of the usual relatively high viscosity (40 per cent iodized poppy seed oil, viscosity of 90 at 20°C., bile of dog, viscosity of 1.8 at 38°C.) empty about one-half spontaneously in from twelve to twenty-four hours when the resistance of the intramural portion of the common bile duct is eliminated by means of a cannula fixed in this portion of the duct. In fasting human subjects little tendency toward spontaneous emptying of the gallbladder is observed. In human subjects on a carbohydrate diet there is a tendency toward emptying of the gallbladder over a period of from twenty-four to forty-eight hours.

The author concludes that the liberation of cholecystokinin (a hormone discovered by Ivy and his collaborators) by the action of fat or of acid in the intestine is the major factor concerned in the contraction and evacuation of the gallbladder that follow a mixed meal. Duodenal motility facilitates this process.—*Karl Kornblum.*

GYNECOLOGY AND OBSTETRICS

Danelius, G., and Heyrowsky, K. Zur Röntgendiagnose des intrauterinen Fruchttodes. (Roentgen diagnosis of intrauterine death of the fetus.) *Arch. f. Gynäk.*, 1932, *148*, 31–42.

A number of roentgen signs of death of the fetus in utero have been described in the literature, among them flattening of the skull and elongation of the skull in the direction of the occiput. Kehrer described this latter sign and calls it the string-purse sign. The Spalding-Horner sign consists of the bones being pushed over each other like the tiles of a roof. Other signs that have been described are a pronounced extension of the spinal column, bending of the head toward the spinal column, marked curvature of the spinal column as a whole or locally, peculiar positions of the extremities and calcium poverty of the bones.

The authors describe 3 cases of death of the fetus verified clinically and give roentgen pictures of them. In Case I the mother was very obese and the roentgenograms were a valuable supplement to the clinical diagnosis. In all three cases there was Spalding-Horner's symptom, the malformation of the skull being so great in the first case that it could be seen during the pains. Flattening of the skull was seen in Case III. Kehrer's string-purse symptom was not seen in any of them. In Case III the child's spinal column was bent toward the skull but the authors have seen a bend of almost 90° in the cervical column in a case in which a normal living child was delivered. Abnormal curvature or extension of the spinal column is often seen in living fetuses. Extension of the spinal column after rupture of the membranes is almost physiological. No conclusions can be drawn as to the death of the fetus from the position of the limbs. The authors did not see calcium poverty of the bones in any of their cases. Possibly the time between the death of the fetus and the taking of the roentgenograms was too short.

Apparently after the child's circulation stops the brain loses its turgor and intracranial pres-

sure falls so that the general internal pressure of the uterus is stronger and pushes the bones over each other. But these roentgenograms must be interpreted carefully as the boundary between a normal and abnormal configuration of the skull is not very sharp and only decidedly abnormal pictures can be considered positive. In one of the authors' last cases though there was no doubt clinically of the death of the fetus none of the characteristic roentgen symptoms of death could be seen. Even examination in two planes perpendicular to each other, which must always be performed in doubtful cases, did not show even any suspicious symptoms.—*Audrey G. Morgan.*

SKELETAL SYSTEM

MOREAU, LAURENT. Considérations radiologiques sur quelques affections osseuses. (Roentgen considerations on certain osseous affections.) *Bull. et mém. Soc. de radiol. méd. de France*, Nov., 1931, *19*, 471–477.

In studying the roentgen appearance of certain bone affections in which a redistribution of the calcium forms the chief manifestation, the author distinguishes between two great groups: (I) those with an inflammatory course, and (II) those with a non-inflammatory course.

I. In the first, two subdivisions are made according to whether there is involvement of (A) the epiphyses or apophyses (so-called epiphysitis or apophysitis) or (B) of the entire bone (total osteitis).

A. Epiphysitis or apophysitis. These include the following conditions: infantile osteochondritis of the hip or the so-called Leg-Calvé-Perthes' disease, tibial apophysitis or Schlatter's disease, patellar apophysitis or Larsen-Johansson's disease, calcaneal apophysitis, epiphysitis of the fifth metatarsal, apophysitis of the greater trochanter, epichondylitis of the humerus or tennis player's disease, metacarpal epiphysitis, lateral apophysitis of the cervical spine, etc.

B. Total osteitis. This includes the tarsal scaphoiditis of childhood, or Köhler's disease and malacia of the semilunar or Kienböck's disease.

II. In the second group, that is, those of non-inflammatory course, a distinction is made according to whether or not the bone condensation is associated with increase in the volume of the bone involved. The use of the term "affections" for the designation of these conditions is not entirely correct, inasmuch as most of them reveal no pathologic symptoms whatever. The bone condensation might appear in the form of solitary focus or in any variation up to a complete condensation of the greater part of the skeleton. Among the conditions without increase of the bone volume are included: osteopoecilia in which "spots" of condensation may occur throughout the entire skeleton, the condensing osteitis of Voorhoeve, in which the condensations are arranged in the form of stripes running parallel to the long axis of the bone, the condensing osteitis of Sicard in which the condensation occurs especially in the spinal column, pelvis and hips and which is associated with more or less pronounced pain, and finally, the eburnating osteosis of Putti in which one single member of one side is involved. The osteopetrosis of Karshner, the marble bones of Albers-Schönberg and the ivoryv ertebrae of Souques may be placed in the group of eburnating osteosis. An association of the bone condensation with increase in the bone volume is observed: in melorheostosis of Léri, in which there is a compact hyperostosis in the form of "candle drips" of the bones of one extremity; in the well-known Paget's disease, with all its varieties, in the hypophyseal dysostosis, also called Schüller's disease or Christian's syndrome, and in leontiasis ossea.

One also may include among the condensing and hypertrophic affections of bone the following related conditions: ossifying periostitis, acromelic periostosis of Marie, poikilo-dermatomyositis, rhizomelic spondylosis, Kümmell-Verneuil's disease, hyperostosing lumbarthria, Pellegrini-Stieda's disease, excessive calcium deposits around fractures, and finally calcification of the nucleus pulposus of the intervertebral discs.

In all the above-mentioned conditions the chief phenomenon is represented by a decalcification and hypercalcification as observed on the roentgenograms. That this is the result of a disturbed calcium metabolism there can be no doubt. The etiology itself, however, is not so important as the pathogenic factor whether this be a repeated trauma, a microbic agent or a diathesis. In all instances a re-arrangement of the calcium within the bone affected takes place. As is well known, the calcium is transported to the bones by the vessels under regulation of the vasomotor nerves, the amount in the blood being dependent on the secretion of the endocrine glands, chiefly of the parathyroids, which control the phosphorus-calcium

metabolism. Thus the author believes that a disturbance in the function of the parathyroids is responsible for most of the affections or anomalies of the skeleton in which a bone condensation is observed. This is a rather intriguing hypothesis but probably insufficient as yet to explain all the changes as observed roentgenologically.—*T. Leucutia.*

Lièvre, J.-A. La classification des dystrophies osseuses et l'ostéose parathyroïdienne. (Classification of osseous dystrophies and the parathyroid osteosis.) *Presse méd.*, Feb. 13, 1932, *40*, 234–236.

In a previous publication the author demonstrated that certain osseous affections, as for example, Recklinghausen's disease, are the result of a mobilization of the calcium of the skeleton by parathyroid adenoma and therefore he suggested that the name of parathyroid osteosis be used for the designation of such conditions. In the present article he tries to coordinate the group with other osseous dystrophies and thus he proposes the following classification: (1) Osteopathies due to deficiency, as for example, osteomalacia, puerperal osteomalacia, rickets and juvenile osteomalacia (which in fact are nearly always manifestations of late rickets); (2) osteitis deformans Paget. The author is of the opinion that, at least from a clinical standpoint, this condition represents a distinct entity, having nothing in common with Recklinghausen's disease; (3) parathyroid osteosis. This affection is the result of liberation of calcium of the bony skeleton under the influence of adenoma of the parathyroid. The liberated calcium is partly excreted, partly deposited in the soft tissues, as for example, viscera, blood vessels, connective tissue, etc. Clinically the condition is characterized by marked pain along the bones, recurring spontaneous fractures with rapidly developing deformities of the skeleton and later by total disability, with very marked softening of all the bones. The visceral signs consist in nephritic colics due to hypercalcuria and precipitation of the calcium within the urinary apparatus, renal insufficiency, digestive disorders, crises of palpitation, tachycardia, very marked asthenia with muscular hypertonia and electric hypoexcitability, hypercalcemia, negative calcium balance, diminution of the blood phosphorus, etc. Without ablation of the parathyroid adenoma the condition terminates fatally. The author distinguishes between a localized form, a renal form, a form with metastatic calcifications and a cachectic form of parathyroid osteosis. Some of the cases show a very long duration and a few may result in spontaneous healing. In conclusion, the author states that one must separate from these morbid entities the nonspecific dystrophies of the bone such as cysts, Pagetoid conditions, giant cell tumors, osteoporosis, etc., which are common reactions of the bone to various processes. —*T. Leucutia.*

Ask-Upmark, E. Further observations on osteitis fibrosa generalisata. *Acta chir. Scandinav.*, 1931, *68*, 551–573.

In a previous article the author discussed the relation between disturbance of the parathyroid glands and osteitis fibrosa generalisata Engel-Recklinghausen, expressing the opinion that the hypertrophy of the parathyroid glands is the primary factor. Since then a new case of osteitis fibrosa generalisata was observed in which likewise a marked enlargement of the parathyroid gland was noted. The history shows that the patient, a woman aged forty-three, suffered for about twelve years from general weakness and anorexia, later resulting in complete inability to walk. During the earlier stages of the disease a diagnosis of osteitis deformans Paget was made which then was changed to osteitis fibrosa generalisata Engel-Recklinghausen. The patient was operated upon but died eleven days later. During the postoperative period a condition developed which was characterized chiefly by decreased blood calcium level, mental disturbances (anxiety, irritability, etc.), and a marked motor hyperactivity, although there was no definite evidence of tetany. It was thought that this syndrome was due to hypoparathyroidism.

In connection with this case the author collected 30 cases from the literature in which parathyroidectomy was performed, and arranged them in a tabular form, indicating the relative size of the parathyroids and the postoperative results, Of these, 3 cases died following the operation, 3 cases remained unimproved and 24 were more or less improved.

In discussing the general treatment, the following precautions are advised: (1) Preoperative measures: The patient should be submitted to operation as early as possible. It is advisable to administer a diet rich in calcium as well as daily doses of codliver oil or viosterol (vitamin D) and several oranges and limes (vitamin C), and to apply ultraviolet radiation for several

weeks. (2) Operative measures: In performing a parathyroidectomy great care must be taken not to remove too much or too little of the parathyroid tissue. (3) Postoperative measures: Continuation of the above preoperative diet associated if necessary with administration of thyroid extract per os, parathormone subcutaneously and calcium chloride intravenously. —*T. Leucutia.*

Bergstrand, Hilding. Ostitis fibrosa generalisata Recklinghausen mit pluriglandulärer Affektion der innersekretorischen Drüsen und röntgenologisch nachweisbarem Parathyreoidtumor. (Osteitis fibrosa generalisata Recklinghausen with pluriglandular affection of the glands of internal secretion and roentgenologically demonstrated parathyroid tumor.) *Acta med. Scandinav.*, 1931, *76*, 128–152.

The author describes in great detail a case of osteitis fibrosa generalisata Recklinghausen in which the bone changes were so slight that the correct diagnosis was made only post mortem. The condition was associated with marked enlargement of two parathyroid glands, one of which gave the impression of an aneurysm at the roentgen examination before death.

The bone process, as determined histopathologically, consisted in an excessive lacunar resorption. The fact that the changes were in such an initial state that they could not be diagnosed clinically proves that they were a secondary manifestation of the parathyroid hyperplasia. It is interesting that the patient otherwise showed a marked picture of hyperparathyroidism consisting in very pronounced loss of weight, general weakness, nervousness, tachycardia, very severe constipation, vomiting, excessive thirst, polyuria and an intermittent clinical course. There was no pain along the bones except some dull ache in the top of the head. In addition to the enlargement of the parathyroids there was a disturbance of the adrenals and thyroid gland, with certain clinical manifestations as, for example, excessive pigmentation of the skin, change in the blood picture, etc. The microscopic examination of the parathyroids showed a diffuse change of the entire parenchyma such as observed in Basedow's struma and not the typical picture of adenoma.—*T. Leucutia.*

Jung, Adolphe, and Hakki, A. Chinassi. De l'influence des opérations parathyroïdiennes sur la calcémie chez l'homme. (The influence of parathyroid operations on calcemia in the human.) *Compt. rend. Soc. de biol.*, Oct. 12, 1931, *108*, 40–42.

In a number of cases of ankylosing polyarthritis and sclerodermia, characterized by hypercalcemia, the authors, in association with Leriche, performed under local anesthesia a series of parathyroidectomies or of resections of the terminal segment of one of the inferior thryoid arteries (including the origin of the three glandular branches). It was found that both operations produced (1) in case of hypercalcemia, a reduction of the calcium level to nearly that of the normal, and (2) in case of normal calcemia, no influence or only a slight lowering of the calcium level.—*T. Leucutia.*

Weiss, A.-G., Monguio, J., and Bernard, L. Influence de la parathyroïdectomie sur le calcium sanguin. (Influence of parathyroidectomy on the blood calcium.) *Compt. rend. Soc. de biol.*, Oct. 12, 1931, *108*, 12–14.

More recently a removal of the parathyroids was advised by several authors in certain conditions such as ankylosing polyarthritis, Recklinghausen's disease and sclerodermia, to reduce the excessive hypercalcemia. The operations consisted either in removal of one or several of the parathyroid glands or in ligation of the inferior thyroid artery.

The authors performed a series of experiments on the blood calcium in cats by using both types of operations. It was found that neither of them influenced the blood calcium level. The removal of all four parathyroid glands provoked a tetany and rapid death before the calcium content could be determined in one cat. These results agree with those of Bourguignon and Sainton but disagree with those of Leriche and Jung. It is therefore advised that one be as yet guarded in making final conclusions.—*T. Leucutia.*

Parhon-Stefanesco, Constance. Augmentation de la tranparence osseuse aux rayons x, à la suite d'injections de la parathormone de Collip. (Augmentation of the bony transparency to the roentgen rays as the result of injections of parathormone Collip.) *Compt. rend. Soc. de biol.*, 1931, *108*, 300–301.

The author injected daily doses of 20 units of parathormone Collip for 36 injections and then of 40 units for 12 injections (total, 1200 units) in an epileptic, and found that roent-

genograms taken at various intervals revealed marked demineralization of the bones. The blood calcium was 110 mg. previous to treatment and 115.5 mg. after eighteen days of treatment. The findings coincide with the clinical findings of other observers, demonstrating that the hyperparathyroid syndrome is characterized, among other things, by a decalcification of bone.—*T. Leucutia.*

Delmas-Marsalet, P. Maladies osseuses et troubles du métabolisme calcique. (Osseous diseases and disturbances of calcium metabolism.) *Presse méd.*, 1932, *40*, 282–287.

During the past four years, the authors have been successful in treating a case of Paget's and a case of Recklinghausen's disease with administration of calcium, and they wish now to use the good results obtained as a proof for the unitarian theory of the two conditions. Both cases are described in lengthy detail and illustrated with numerous roentgenograms taken before and after treatment. The interesting feature is that the calcium was administered in the form of gluconate and associated with the administration of irradiated ergosterin (irrastérine). The procedure in the Paget's case was as follows: First series from March 28 to June 28, 1930; daily 50 drops of irradiated ergosterin per os, and a total of 60 intragluteal injections of calcium gluconate (30 daily injections, then a rest of 15 days, a second series of 30 injections and a second rest of 15 days); second series from June 29 to August 11, daily 60 drops of irradiated ergosterin and a total of 18 injections of calcium gluconate (3 per week); third series from September 9 to 21, 1930, daily 60 drops of irradiated ergosterin and daily 60 drops of solucalcine; fourth series from September 23, 1930, to July 23, 1931, daily two teaspoonfuls of granulated calcium gluconate and 5 drops of irradiated ergosterin. The course of treatment in the Recklinghausen's disease was somewhat similar; the case, however, was treated four years ago and thus the result obtained is of longer duration.

These two cases are interesting because recovery was obtained by simple improvement of the calcium metabolism. It is the author's opinion that the reason why other calcium preparations have failed to bring about a similar effect lies in the non-absorption of those preparations. The calcium gluconate gives up a slightly acid radical (gluconic acid) whereas the chlorides, phosphates and lactates of calcium yield radicals which are more acid and consequently more decalcifying. The gluconic acid, producing oxidation of the glucose, is entirely utilized and, especially when administered in association with massive and prolonged doses of vitamin D, has an extraordinary power of recalcification. It is recommended that in all cases of Paget's and Recklinghausen's disease, the following standard treatment be tried for a period of at least six months: (1) vitamin D in oily solution in a daily dose of 7,500 antirachitic rat units administered twice in cold milk; (2) three teaspoonfuls (that is about 12 grams) of pure calcium gluconate either in powder or granules. An intramuscular injection of 1 gram gluconate of calcium in a 10 per cent solution three times per week.

A control examination is made by means of roentgenograms every three months. It seems that the same procedure is indicated in osteomalacia and leontiasis ossea.—*T. Leucutia.*

Noble, T. P. Generalized osteitis fibrosa cystica associated with a parathyroid adenoma. *J. Bone & Joint Surg.*, 1932, *14*, 181–185.

Noble reports a case of generalized osteitis fibrosa cystica occurring in a Chinaman due to a parathyroid adenoma. The parathyroid tumor was found neither by clinical examination nor at operation, but was revealed at postmortem examination. He recommends surgical exploration of the parathyroid glands in cases of generalized skeletal decalcification if associated with hypercalcemia. He briefly reviews the symptomatology of the condition together with the therapy employed and refers to the extensive reviews on the subject which have appeared by Hunter in England and by Barr and Bulger in America.—*R. S. Bromer.*

Camp, John D., and Ochsner, Harold C. The osseous changes in hyperparathyroidism associated with parathyroid tumor: A roentgenologic study. *Radiology*, July, 1931, *17*, 63–69.

The roentgenographic changes observed in the osseous system in two cases of hyperparathyroidism associated with tumor of the parathyroid glands are presented. The osseous changes in roentgenograms consist of generalized osteoporosis, cystic lesions, and deformities. The generalized osteoporosis is characterized by a miliary or granular appearance. This change is best observed in the skull and appears to be peculiar to hyperparathyroidism. In addition,

the bone trabeculae and cortical bone are thinned, and areas of subperiosteal absorption are seen in the long bones and phalanges. Single or multiple cystic lesions are found in the jaw, pelvic bones, and long bones. These lesions are often confounded with those of osteitis fibrosa and with giant cell tumor. The deformities due to softening of the bones consist of kyphosis, narrowing of the pelvis, coxa vara, bowing of the legs, and infractions. It is not unlikely that pathologic fractures may even occur. In addition, renal calculi are not uncommonly found. In each instance, removal of a parathyroid tumor was followed by a definite arrest of decalcification and progress toward restoration of normal bone structure, as observed roentgenographically.—*Authors' abstract.*

Loewy, Georges. Dérivation totale de la bile hors du tube digestif, hypertrophie des parathyroïdes, ostéomalacie. (Total derivation of the bile outside the digestive tube; hypertrophy of the parathyroids; osteomalacia.) *Presse méd.*, Nov. 7, 1931, *39*, 1627–1630.

All investigators who succeeded in keeping the experimental animals alive after biliary fistulae draining the bile elsewhere than in the digestive tract noticed that disorders of the calcium metabolism occurred consisting chiefly in broken ribs, spontaneous fractures, fusiform thickenings at the level of healed fractures, rarefaction of the spongious tissue of the epiphyses, etc.

The author was able to observe a dog which lived fifteen months after choledoco-ureteral anastomosis, this permitting a minute study of the calcium metabolism as well as of the changes of the bones. The animal was then sacrificed and a post-mortem examination done. The findings both during life and after death are described in detail.

It is notable that the total derivation of the bile into the ureter was exceedingly well tolerated by the animal. The appetite remained good and the nutrition was normal, if one may judge from the general appearance and activity of the dog. The only abnormal phenomenon was the repeated appearance of intestinal hemorrhages. The autopsy revealed important alterations of the duodenal mucosa, however without evidence of ulceration. The mucosa of the ileum presented intensive vascular congestion which no doubt was responsible for the repeated hemorrhages observed clinically. There was no evidence of chronic nephritis. The skeleton demonstrated a progressive osteomalacia. The parathyroids were uniformly hypertrophied, due to considerable hyperplasia of the glandular elements, however without inflammatory reaction.

Repeated determinations of the calcium content of the blood during the fifteen months gave an average value which was nearly normal. According to the author this apparently normal behavior is due partly to the preservation of the gallbladder which, as is known, absorbs some of the calcium of the bile, and partly to the replenishment from the reservoir of the osseous epiphyses, this latter eventually leading to osteomalacia. The hypertrophy of the parathyroids is explained by the fact that of all organs, they are the most sensitive to ionic disequilibrium of the calcium in the blood serum. It is most probable that the increased secretion acts in a manner similar to the experimental injection of the parathyroid hormone, mobilizing the reserve calcium of the epiphyses.

In summarizing, the conclusion is reached that the prolonged derivation of bile leads through different mechanisms to a loss of the molecular calcium and thus to an ionic disequilibrium of the blood serum, resulting in hyperplasis of the parathyroids. The exaggerated secretion of the parathyroids provokes a mobilization of the calcium of the epiphyses with demineralization and osteomalacia. The decalcification occurs without the aid of osteoclasts. —*T. Leucutia.*

Péhu, M., Policard, A., and Dufourt, André. L'ostéopétrose ou maladie des os marmoreéns. (Osteopetrosis or marble bone disease.) *Presse méd.*, 1931, *39*, 999–1003.

The condition was first described in 1904 by Albers-Schönberg who used the term "marble-bone disease." A perusal of the literature reveals that since then about 30 cases have been added, but that not one has occurred in France. Karshner, in 1926, was the first to suggest the term "osteopetrosis," which, according to the authors, is to be preferred. Other names such as osteosclerosis, osteopathia hyperostotica (sclerotisans) multiplex infantilis, etc., have also been used.

The authors had the opportunity to observe the first case in France. In connection with this case, they accumulated all the data from the literature and in the present article they describe the disease in a comprehensive manner, discussing in detail the clinical characteristics,

history, etiology, pathogenesis, diagnosis, and therapy

Briefly, the history of their case was as follows: The boy was first seen at the age of twenty-seven months (June 14, 1923) because of marked pallor and retarded walking. There was a large skull with enlargement of the spleen and liver and with a marked anemia, suggesting a diagnosis of splenic anemia. An antisyphilitic treatment was started, this being continued for a period of three years without any result. In 1924, nystagmus, a little later exophthalmos and a progressive diminution of vision developed. In 1927, there was evidence of a bilateral optic atrophy. In 1929, the anemia became more severe. At this time a general examination was made and a deformity of several bones was discovered. Roentgenograms of the entire skeleton revealed a typical condition of marble bone disease. Five days later, the boy died with signs of an extremely severe anemia. At autopsy, a very large liver (970 mg.) and spleen (250 gm.) were found associated with extensive bone changes and with adenoma of the parathyroids. This latter is of special significance since it might constitute the *primum movens* in the pathogenesis of the disease.

In summarizing, the chief characteristics of osteopetrosis are the typical marble appearance of the bones as evidenced in the roentgenograms, occurrence of multiple fractures, a progressively developing anemia depending on the extent of the bone marrow involvement, progressive narrowing of the visual fields, retardation of development, and defective teeth. Although not all of the reported cases were followed up, it appears that the condition is more benign in adults (1 death in the 12 cases in the literature) and quite malignant in children (13 deaths in the remaining 18).

In discussing the therapeutic aspect of the disease, the authors express the opinion that partial parathyroidectomy might prove a valuable procedure.—*T. Leucutia.*

Lièvre, J.-A., and Muller, P. Un cas d'adénome parathyroïdien avec lésions diffuses du squelette. (A case of adenoma of the parathyroid with diffuse lesions of the skeleton.) *Bull. et mém. Soc. méd. de hop. de. Par.*, Oct. 26, 1931, *55*, 1515–1522.

The authors report a case of parathyroid disease followed from the beginning of the disease until death five years later. The condition was in a woman and began at the age of forty-one with pains in the lower extremities. A fracture of the right femur occurred a year later. This was treated by extension for two months without union. A roentgenogram at this time showed little evidence of callus and marked osteoporosis of the bone. There was reticulation of the cortex, the result of many small cavities. The medullary cavity was enlarged. A biopsy showed friable osseous tissue which was reported by the pathologist to be characteristic of von Recklinghausen's disease. Roentgenograms showed marked decalcification of the other bones of the body. Two years later there were spontaneous fractures of the left femur and right humerus. Roentgenograms taken at this time and at intervals showed progressive decalcification with bowing and deformities of the bones. The skull showed progressive decalcification. Clinically, there was progressive weakness, later anorexia, constipation, and gastric crises. Syphilis, as evidenced by a strongly positive Wassermann reaction, was treated early in the course of the disease. There was marked hypercalcemia, and excessive calcium in the urine. Exploration of the parathyroids was refused. Autopsy showed an adenoma of the parathyroid behind the right lobe and body of the thyroid.—*M. T. Harris.*

Jaffe, Henry L., Bodansky, Aaron, and Blair, John E. Fibrous osteodystrophy (osteitis fibrosa) in experimental hyperparathyroidism of guniea-pigs. *Arch. Path.*, Feb., 1931, *11*, 206–228.

In a previous report the authors described the production of osteitis fibrosa as a result of experimental hyperparathyroidism in dogs. In this paper they studied the effects of parathyroid extract (parathormone Collip) on the bones of guinea pigs, inasmuch as guinea pigs had been reported "immune" to the action of parathormone. This conclusion was based on the absence of effect on the serum calcium following the injection of parathormone.

The authors' summary is as follows: The subcutaneous injection of one large single dose of parathormone into a young guinea pig produces severe and rapid decalcification of the skeleton in forty-eight hours. Age, also, seems to be a factor in the production of lesions after single injections of parathormone. Adult guinea pigs given injections (20 units per hundred grams of body weight) did not show changes in the bones forty-eight hours after the injection. After repeated daily injections of smaller doses

of parathormone, resorption of bone and fibrosis of bone and marrow result. The lesions observed after daily injections of parathormone into guinea pigs are of the same order as those described for ostëitis fibrosa without osteoid tissue in man. Osteoid tissue and cysts in the marrow may appear during the repair of severe lesions in experimental hyperparathyroidism of guinea pigs.—*R. S. Bromer.*

GENERAL

Lindén, Oskar. Weichteilverkalkungen nach Chinininjektione. (Calcifications of the soft parts after injections of quinine.) *Acta radiol.*, 1932, *13*, 57–63.

Two cases of calcareous infiltration, one in the soft tissues of the gluteal region and the other in the upper part of the hip following quinine injections for malaria are described and illustrated with roentgenograms. Differential diagnosis from encapsulated parasites may be necesary in such cases but in both these cases such parasites could be definitely excluded.—*Audrey G. Morgan.*

ROENTGEN AND RADIUM THERAPY

Taussig, Albert E., and Schnoebelen, Paul C. Roentgen treatment of agranulocytosis. *J. Am. M. Ass.*, Dec. 12, 1931, *97*, 1757–1761.

Schultz's definition of the disease included angina, prostration, jaundice, normal red blood picture, normal platelets, extreme leucopenia with almost complete absence of granules, no tendency to hemorrhage, and fatal ending. This must be modified since several of the findings are inconstant. Agranulocytosis has been observed in phlegmonous tonsillitis, septicemia, influenza, Hodgkin's disease, malaria, in kidney tumor, and after typhoid vaccine.

Agranulocytosis has ceased to be a rare disease and 334 cases have been collected and analyzed. However, no agreement has been reached as to proper therapeutic measures. No one, except Friedemann with his 43 cases, has had enough experience to be justified in drawing conclusions from his own experience. His method of irradiating the long bones with small doses of roentgen rays, the daily dose being about one-twentieth of an erythema, is the most promising one known at present.

The author presents 4 cases which demonstrate the value of roentgen therapy. Two of the cases showed that the agranulocytic process preceded the sore throat and he concludes that the blood condition is primary to the angina.—*E. W. Hall.*

Conner, H. Milton, Margolis, Harry M., Birkeland, Ivar W., and Sharp, John E. Agranulocytosis and hypogranulocytosis. *Arch. Int. Med.*, Jan., 1932, *49*, 123–150.

Agranulocytosis is applied to that condition in which there is complete, or almost complete, absence of granular leucocytes, accompanied by leucopenia and relative increase but, in most instances, absolute decrease of lymphocytes. Hypogranulocytosis is that condition in which there is less marked reduction in the number of granular leucocytes and well marked leucopenia, without absolute increase in the number of lymphocytes but with relative lymphocytosis.

There has been much discussion in the literature as to the existence of a distinct clinical entity, agranulocytic angina, as described by Schultz. The tendency at the present time is to consider the agranulocytosis as a symptom.

Agranulocytosis and hypogranulocytosis conceivably may occur as a result of defective formation of granulocytes, from their abnormal destruction, or from their improper distribution or delivery into the circulation. The consensus of opinion in the literature is that these conditions are usually due to defective myeloblastic function of the bone marrow, and this is the opinion of the authors.

Fourteen cases are reported in considerable detail, several with pathological reports. Seven cases presented a clinical syndrome that corresponded, in most details, with that described by Schultz as agranulocytic angina, 3 others probably belong in this group. The symptoms were diverse and the situation of the lesions was various. No common etiologic factor appeared in these cases. Various types of organisms were recovered from the lesions presented by these patients. In none was there a history of exposure to any of the chemicals or physical agents known to produce agranulocytosis. All presented evidence of an infection to which there seemed to be little resistance.

Pathologically the characteristic features noted in these cases were marked aplasia of the bone marrow and lack of the cellular reaction that is usually observed about regions of necrosis and infection. The peculiar inflammatory

reaction that was observed seemed to be merely a consequence of the absence of circulating granular leucocytes.

When the peculiar blood picture here described is found, a careful search for all possible causes should be made. Particular care should be given to the diagnosis of well-recognized diseases that are associated with leucopenia and great reduction of granulocytes, such as aplastic anemia, acute leucemia, pernicious anemia in an aplastic phase, and metastasis to bones. Careful inquiry should be made regarding intoxication from benzene, the use of roentgen rays and radium, and the administration of arsenicals. Infectious mononucleosis, chronic or acute lymphatic leucemia with low leucocytic values and monocytic leucemia should be looked for. Particular attention should be called to the value of the reticulocyte and platelet counts.

The prognosis is extremely poor in any condition in which agranulocytosis develops. Few patients have recovered if the leucocyte count has fallen below 1000 in each cubic millimeter of blood. Treatment has consisted of the administration of leucocytic extract, gentian violet, and acriflavine, given intravenously; transfusions; roentgen irradiation; extract of bone marrow, and fetal liver. In some cases specific treatment was not administered. The results with various methods of treatment were inconclusive.—*Karl Kornblum.*

Holthusen, H., and Engelmann, K. Die Gefahr der Röntgenkarzinoms als Folge der Strahlenbehandlung. (The danger of roentgen carcinoma as a result of therapeutic irradiation.) *Strahlentherapie*, 1931, *42*, 514–531.

The authors describe a case of roentgen carcinoma of the cheek which developed nineteen years after irradiation for sycosis barbae. The treatment had been followed by a chronic roentgen dermatitis which finally developed into cancer. They also give brief abstracts of 39 cases from the literature. They conclude that roentgen carcinoma after therapeutic irradiation with the present methods is very rare. Only 3 of these cases occurred after 1910. Most of the cases of roentgen carcinoma are in roentgenologists or technical workers in roentgen laboratories who are exposed to the rays repeatedly over long periods of time. There is little danger with a single large dose or even with the protracted fractional method in which the total dosage is given within a few weeks. If the nature of the disease is such as to require a frequent repetition of irradiation there is some danger of cumulative injury but this is at present decreased by the fact that the doses for the individual irradiations are much less than they formerly were, and as the danger of cumulation is known the dosage can be regulated accordingly.

The distribution of roentgen carcinoma is not the same as that of roentgen skin injuries. Skin injuries are most frequent on the abdomen and buttocks on account of the large number of irradiations in gynecological cases but by far the greatest number of roentgen carcinomas are seen on the head, followed next in sequence by the vulva and anus. The head seems to show a similar predisposition to carcinomas developing in the scars of burns.—*Audrey G. Morgan.*

Rost, G. A., and Keller, Ph. Einwirkung von Röntgenstrahlen verschiedener Quälitat auf die Psoriasis. (Effect of roentgen rays of different qualities on psoriasis.) *Strahlentherapie*, 1931, *42*, 539–543.

Skin erythema is not an accurate measure of skin tolerance or of therapeutic effect; the authors therefore tested the effect of different qualities of rays on foci of psoriasis. It is easiest to determine the threshold value of effect on old stubborn foci; young fresh papules are not so well adapted for the purpose. Adjacent places on large psoriatic areas were irradiated with different qualities of rays and the equivalent dosage determined by observing the effect for a long period. As fields not larger than 4 sq. cm. were used the effective dose was the same as the incident dose, for the secondary irradiation is so slight as to be negligible. Half-value layers from 0.3 mm. to 12.0 mm. aluminum were tested. Rays of 0.3 mm. half-value layer were found the most effective. With the soft rays the antipsoriatic action was also accompanied by erythema of the surrounding skin, which was not the case with the hard rays. The dosage given was generally 100 R three times in ten days but foci of psoriasis can also be healed with a dose of 300–400 R with a half-value layer of 0.5 given at one dose, though with doses of 600 R there is sometimes rapid recurrence.

The authors are not prepared to say just what conclusions can be drawn from the superiority of the soft rays in psoriasis. But

at least they can recommend the soft rays as harmless for use on the scalp for with three applications of 100 R in ten days they were able to cure psoriasis without the hair falling out, while when rays with a half-value layer of 0.5 mm. were used the hair fell out. The soft rays are also to be preferred in psoriasis in small children as the deep tissues are spared.

The soft rays have the disadvantage that it is very hard to determine dosage with Sabouraud tablets for this is the region in which Sabouraud tablets are most dependent on wave length. An ionization instrument independent of wave length should be used in determining dosage.

Soft rays of about 0.3 mm. half-value layer have the advantage over grenz rays in that they can be given in a much shorter time, permit of the use of larger fields and dosage can be determined more accurately.—*Audrey G. Morgan.*

Brocker, W. Die Behandlung der Röntgenverbrennungen mit langwelligen Strahlen. (Treatment of roentgen burns with infra-red rays.) *Strahlentherapie*, 1931, *42*, 551–570.

Experimental work has shown that the application of infra-red light before and after irradiation does not affect the reaction of the human skin to roentgen irradiation and in animal experiments infra-red rays did not have any prophylactic action in preventing roentgen injuries. The development of ulcers could not be prevented by infra-red irradiation given either before or immediately after roentgen irradiation. But infra-red irradiation is an excellent means of treating roentgen burns after they have developed. Two cases are described in which roentgen burns were cured by infra-red irradiation after other methods of treatment had failed.—*Audrey G. Morgan.*

Hazen, H. H. The cause and prevention of radiodermatitis. *J. Am. M. Ass.*, Dec. 19, 1931, *97*, 1881–1885.

Of 111 cases of radiodermatitis, 3 resulted from taking of roentgenograms, 13 from high voltage therapy, 7 occurred in roentgenologists, 13 from treatments in beauty shops, and 75 from superficial therapy. Sixty-six were the result of therapy by dermatologists and 22 by roentgenologists. Ninety-seven showed signs of injury within the first year. Four showed nothing for three years and 2 for four years.

Many of these patients were unsuited for irradiation such as those with hypertrichosis, tinea cruris of the scrotum, primrose dermatitis, large pigmented nevi and lupus vulgaris. Some were given too frequent irradiation and some too great a total dosage.

The study suggests careful selection of patients, modern standardized apparatus, avoidance of irritating drugs, and care that treatment by other physicians is not overlooked. Radium should always be filtered through rubber or aluminum. The study also indicates lessened, harmful results by use of fractional doses and avoidance of erythema except in malignancies and warts. No more than three epilations of the scalp are permissible and total skin dosage over a period of years should not exceed two and one-half units for dry and four and one-half units for greasy skins.—*E. W. Hall.*

Hayer, E. Zur Frage der Behandlungsmethode der Thyreotoxicosen. (Method of treatment of thyrotoxicoses.) *Strahlentherapie*, 1931, *42*, 414–424.

The object of local treatment in thyrotoxicosis is to decrease the secretion of the thyroid, on the theory that it is having a toxic action on the organism. This can be accomplished by surgery or roentgen treatment. The action of surgery is rapid but dosage cannot be controlled and the average operative mortality is 9.6 per cent. Roentgen irradiation also decreases the secretion by inhibiting the function of the secretory cells. Direct cell destruction has not been demonstrated histologically and there is no decrease in the size of the thyroid.

The essential point in roentgen treatment is decrease in function which can be brought about by small doses of 40–60 R. But after such small doses the injury is soon compensated and function may rise to a higher level than it was before. Gradually increasing doses must be given until the inhibition of function has become permanent. This makes the treatment much longer than surgical treatment. Roentgen therapy, on an average, requires two years and during this time the function of the gland is gradually adapted to the needs of the organism. But the patient is really sick only during the first three months. During this time there is great subjective improvement and internal treatment can be given for the general condition, particularly the circulation. The increase in weight and decrease in basal metab-

olism values are good measures of improvement. The patient is still in a very labile condition, however, and further treatment is required to consolidate the results. Final cure is shown by complete freedom from symptoms, ability to work, low basal metabolism values and uniform weight. Sometimes the patients show headache, dizziness and sleeplessness after irradiation of the thyroid and thymus. In such cases the hypophysis is also irradiated from two temporal fields, the irradiation being repeated 2–3 times at intervals of six to eight weeks.

The author gives tables showing his results in 76 cases. They are divided into 3 groups: the first very severe cases with an increase in basal metabolism of more than 70 per cent, the second moderately severe cases with a basal metabolism of between 40 and 70 per cent and the third mild cases with an increase of less than 40 per cent. In the first group of 24 cases 9 were cured, or 37.5 per cent, the same number were considerably improved, 4, or 16.6 per cent, were not improved and 2, or 8.4 per cent, died. In the second group of 35 cases, 11 were cured, or 31.4 per cent, 20 were improved, or 57.1 per cent, 3 were not improved, or 8.6 per cent, and 1 died. In the third group of 17 cases, 4 were cured, or 23.5 per cent, 8 were improved, or 47.1 per cent, 4 were not improved, or 23.5 per cent, and 1 died.

It was surprising that there were more cures in the severe than in the mild cases but in the latter there was a decided psychic component. There was a large number of cases in the second group that were only improved. These had severe circulatory disturbance when they came for treatment and the residual symptoms were due to lesions of the myocardium. The deaths were not due to the treatment. These patients came for treatment in such bad condition that operation could not be performed and they died within the first two weeks of treatment, 2 of cachexia, 1 of heart failure and 1 of apoplexy. They had only been given a single series of 60–150 r per field.

Definite judgment cannot yet be passed on the value of roentgen treatment in thyrotoxicosis. The choice of cases does not depend so much on the severity of the clinical symptoms as on the nature and extent of the thyroid enlargement. True goiter, particularly the nodular form, cannot be cured by irradiation, which may even cause an early reactive enlargement and lead to temporary signs of compression. Surgery is preferable in such cases, but irradiation may be used in all others.—*Audrey G. Morgan.*

Gantenberg, Robert. Zur Strahlenbehandlung der thyreotoxicosen. (Radiotherapy of thyrotoxicoses.) *Strahlentherapie*, 1931, *42*, 401–413.

The author reports the results of roentgen therapy in 93 cases of thyrotoxicoses, 64 of them being cases of typical Basedow's disease and the other 29 cases of hyperthyreosis. Three fields 6×8, 8×10 and 10×10 cm. were irradiated with a focus-skin distance of 30 cm., 180 kv., 3 ma. and a filtration of 0.5 mm. copper and 1 mm. aluminum. The right and left lobes of the thyroid were irradiated separately with 20 to 30 per cent of a skin erythema dose, only 10 to 20 per cent being used in acute, severely toxic cases. The thymus was irradiated over a field 6×8 cm. in size with 30 per cent of a skin erythema dose. Intervals of two to three days were left between the irradiations. The average total dosage to a series was 70–90 per cent. Intervals of four to eight weeks were left between the series or if necessary more. The results were controlled by basal metabolism determinations.

Even using very strict standards as to results there was cure or very great improvement with ability to resume work in about half the cases and even in the true Basedow cases there was cure in the strictest sense of the word in about 20 per cent. Therefore roentgen therapy may be tried in all cases in which there are not signs of compression that call for immediate operation. If the cases do not show marked improvement in three or four or at most six months they should be operated on, and operation should also be performed in acute cases in which insufficiency of the heart is threatened. In all other cases of thyrotoxicosis roentgen therapy, associated with appropriate internal medication, is the treatment of choice.—*Audrey G. Morgan.*

Haag, F. E., and Schreus, H. Ueber die Röntgenbehandlung des Heufiebers. (Roentgen treatment of hay fever.) *Strahlentherapie*, 1931, *42*, 485–491.

In 1930 the authors treated 9 cases of hay fever with roentgen rays. Five of them were improved, some of them very remarkably. In 1931 reports were received from 8 of them and the improvement had persisted in 4 of the

5 improved cases. There had been recurrence in 1. In 1931 they treated 16 more cases with good results in 6, temporary improvement in 1, no improvement in 8 and result unknown in 1.

Prophylactic or early irradiation is more effective than late treatment. The nose is irradiated with 120 r, 0.5 mm. copper filter and the dose repeated 2 or 3 times with intervals of two or three days. No other treatment was given with the roentgen therapy. About 200 hay fever patients were tested with grass pollen extracts and sensitiveness was found to run parallel with the seriousness of the disease. Patients with severe hay fever showed either nonspecific reactions to all the pollen extracts or markedly specific reactions to a number of them, while patients with mild cases generally showed no reaction to the individual extracts but only a more or less marked reaction to a concentrated extract of mixed grasses.

The reactions were tested before and after roentgen treatment. One patient who was sensitive to only one grass showed no reaction after roentgen treatment. Two others showed no reaction after treatment but unfortunately they had not been tested before treatment. In 5 patients the skin reaction was not completely abolished but was much weaker after treatment. They also improved clinically. In 3 cases there was no change in the skin reactions and also no clinical improvement.—*Audrey G. Morgan.*

Grävinghoff, W. Zur Röntgenbehandlung des kindlichen Asthmas. (Roentgen treatment of asthma in childhood.) *Strahlentherapie*, 1931, *42*, 492–496.

Opinions differ as to the value of roentgen treatment in asthma in childhood. Waldbott in 1928 reported 39 children with allergic asthma treated with roentgen rays with success in 39.4 per cent, while Pritzel in 1930 reported 78 per cent cures lasting up to six years in 100 children treated by irradiation of the thyroid. The thorax and spleen seem to be the preferred fields of irradiation by most authors. Some authors divide the cases into allergic and non-allergic but apparently the results do not differ essentially in the two groups.

The author believes a clinical classification is more valuable. He divides the cases into two groups. The first group have asthmatic bronchitis or typical attacks of asthma in childhood but show a tendency to recover spontaneously at about the age of puberty. They are children with an exudative diathesis and have repeated nasopharyngeal infections. In the other group, the asthma persists into adult life if not treated. They have severe bronchial asthma with a decided tendency to involvement of the nervous system. Typical asthmatic attacks begin in early childhood. In 47 per cent of these cases the children had neurogenous eczema as compared with 3 per cent in the first group. There is a family taint in a higher percentage of the cases than in the first group.

It is not definitely known whether roentgen rays act in asthma by affecting allergic processes, by affecting the vegetative nervous system, as a nonspecific stimulant therapy or by affecting the acid-base balance.—*Audrey G. Morgan.*

Ludin, Max. Beitrag zur Röntgenbehandlung der Lungenaktinomykose. (Roentgen treatment of actinomycosis of the lungs.) *Strahlentherapie*, 1931, *42*, 466–470.

A few successful cases of roentgen treatment of actinomycosis of the lungs have been reported in the literature but most of the cases reported have been failures. In all the cases that have been failures the authors say that method has failed in spite of intense irradiation. The author suggests that the failure may have been because of, and not in spite of, the intense irradiation. He treated 2 cases with very large doses with poor results in both, but in this article he reports a very successful case with small dosage. In pulmonary tuberculosis large doses are known to be injurious while small ones are effective.

In this case cross-fire irradiation was given from 4 fields, anterior, lateral and posterior, over the affected part of the lung. One field each was irradiated on Nov. 26, 28, 30 and Dec. 2, 1929, with a dose of 200 r; size of fields 10×10 cm., focus-skin distance 25 cm., filter 8 mm aluminum, 160 kv., half-value layer 0.55 mm. copper. The patient improved very rapidly after the first series of irradiations. The fistula closed and the cough, fever and stabbing pain disappeared. After a three months' stay at Davos the patient was given a second series of irradiations of the same kind. She was also given potassium iodide treatment. She recovered completely and is now well two years after the beginning of treatment. The only sequel of the disease is a slight shadow of the left phrenico-costal angle as a result of pleuritic induration.

Of course one case is not conclusive but the author thinks treatment with lower dosage should be tried in actinomycosis of the lungs.—*Audrey G. Morgan.*

de Backer, Paul. Klinische Daten betreffend die präoperative und die postoperative Bestrahlung des Brustkrebses. (Clinical data in regard to the preoperative and postoperative irradiation of cancer of the breast.) *Strahlentherapie*, 1931, *42*, 744–752.

The author has given up preoperative irradiation entirely, since if it is successful operation is unnecessary and if not it is dangerous; it mobilizes the more resistant cancer cells and increases the danger of metastasis.

Among 51 cases treated postoperatively before 1925 by implantation of radium tubes in the tissues 10 patients are alive and in good health after at least six years. Many desperate cases were treated by this method because at that time the value of postoperative roentgen treatment was overestimated and cases were operated on that were really not operable. Among 21 patients treated by roentgen therapy alone either before or after operation 6 are in good health after more than eight years, or 28.5 per cent. Three of those who died remained well for at least six years, making a recovery for six years in 42.9 per cent of the cases. Among 20 cases treated more than three years ago with radium applied externally to the subclavicular fossa and the region of the internal mammary combined with fractional roentgen irradiation of the field of operation with moderate doses 10 are still in good health, or 50 per cent.

The technique of irradiation which injures the tissues least seems to be the best; therefore the author has given up the implantation of roentgen tubes and needles in the tissues as this furthers necrosis and infection of the tissues and does not give a homogeneous irradiation.

The results of roentgen and radium irradiation are not good enough so that early cases of cancer of the breast should be treated by irradiation alone without operation. But in inoperable cases irradiation alone should be used and the limits of operability should not be extended too far. The results of diathermy in inoperable cases are now being tested. Since he has been giving postoperative irradiation the author has noticed that recurrences around the brachial plexus disappear almost completely and that large ulcerated recurrences in the scar which are ordinarily a source of hemorrhage and infection are also cured.—*Audrey G. Morgan.*

Lee, B. J., Pack, G. T., Quimby, Edith H., and Stewart, F. W. Irradiation of mammary cancer, with special reference to measured tissue dosage. *Arch. Surg.*, March, 1932, *24*, 339–410.

In this comprehensive article, the authors present a study of 130 cases of primary operable and inoperable carcinoma of the breast which have been treated with measured tissue doses of radiation, expressed in terms of skin erythema units. The patients were divided into various groups, some of which were treated by roentgen rays only, others by external irradiation with the 4 gm. radium pack, others by interstitial irradiation alone, and still others by various combinations of external and interstitial irradiation. In the primary operable cases, most of the breasts and axillary contents were removed surgically at variable intervals after the completion of treatment and whole sections of the breasts were subjected to thorough microscopic study. In this way the radiosensitivity of mammary carcinoma was determined in terms of biologic units of measurement and the tissue changes produced by the various methods of irradiation were carefully studied.

From these studies the authors conclude that preoperative irradiation of mammary carcinoma is of distinct value, in that tumors so treated frequently regress and that in most of the cases better clinical end-results are achieved. The authors stress the fact that an efficient devitalizing dose of radiation cannot be delivered by external irradiation alone, but that to obtain an efficient dose interstitial irradiation must be used. Hence they feel that a combination of external and interstitial irradiation is desirable in the preoperative treatment of these cases, and many of the cases presented in this study were treated in this way. It is shown that to devitalize and destroy mammary carcinoma, especially the radioresistant types, a tissue dosage of 12 skin erythema units must be delivered throughout the tumor, and it is advocated that all mammary cancers should receive this dosage. The various steps in the calculation of the tissue dose are given by the authors, together with useful and accurate tables for computation.

In treating mammary cancer with preopera-

tive irradiation, the latter should be given within a period of three weeks or less, during which time the external irradiation is given in the form of roentgen therapy or the radium pack, followed by the implantation of radon seeds. Six weeks after the interstitial irradiation is the optimum time for radical amputation of the breast, because this interval allows the effects of irradiation to become complete, it permits complete destruction of the tumor and wound healing is unimpaired by the preceding irradiation.

The pathologic studies in connection with this series of cases show that the roentgen rays and radium exert different effects on mammary cancer. The former, used as external irradiation, effects pathologic changes in the tumor chiefly by vascular damage. Radium, used as interstitial irradiation, produces its chief effect by causing direct changes in the tumor cells themselves. Hence both forms of irradiation are desirable in the preoperative treatment of these lesions. The pathologic studies further showed that mammary cancers vary markedly with respect to radiosensitivity, and the authors are able to grade the various types of mammary malignancies with respect to their susceptibility to irradiation.

Optimism is expressed concerning the future treatment of mammary cancers solely with external and interstitial irradiation and without resort to subsequent surgery. Apparently not enough experience has as yet been accumulated to justify this form of therapy as a routine procedure and hence the authors feel that for reasons of safety irradiated breasts should be removed surgically. Keynes' method of irradiating breast carcinoma with needles containing radium element is briefly discussed and the authors feel that one of the chief objections to this method is the difficulty in calculating the correct tissue dosage for malignant masses.—*M. L. Allen.*

Frik, Karl. Zur Röntgenbehandlung der Hypophysentumoren. (Roentgen treatment of tumors of the hypophysis.) *Strahlentherapie*, 1931, *42*, 437–452.

The use of roentgen therapy in the treatment of tumors of the hypophysis has been increasing in recent years but some authors still hold that it loses valuable time and defers operation until it is too late. The author describes 6 cases in which roentgen therapy was used with good results. He believes that irradiation is indicated in all tumors of the hypophysis unless immediate operation is necessary in order to save life. Operation is dangerous to life and the results of radiation therapy are so good that surgery is not justifiable unless absolutely required. Even if a tumor does not respond to a first series of irradiations the treatment should not be discontinued unless an urgent indication for operation develops. In one of his cases permanent improvement of a considerable degree was brought about in the visual disturbances after five series of irradiations given over a period of two years. Rapid development of visual disturbance is not a contraindication to roentgen therapy as shown by one of the author's cases in which there was total blindness on the left and temporal hemianopsia on the right when the patient came for treatment. Optic atrophy had not yet occurred. After three months' roentgen treatment both visual fields were normal. It is not true therefore that only recent cases are benefited by roentgen treatment.

The dosage depends on the individual case, and the details of technique are given for each of his cases. The treatment should be begun cautiously. Fractional dosage is the method of choice. He has never seen any really serious by-effects from roentgen treatment. In 2 of the cases only temporary partial improvement was attained by the treatment. One patient was operated on and died immediately after the operation. The tumor was a large adenoma. The other patient died as a result of the tumor. Both of these were very large tumors and roentgen examination had shown severe changes in the sella.—*Audrey G. Morgan.*

Kohlmann, Gerd. Die Röntgentherapie des Zentralnervensystems. (Roentgen treatment of the central nervous system.) *Strahlentherapie*, 1931, *42*, 453–465.

Inflammatory diseases of the brain and spinal cord are first considered. Roentgen therapy has proved very effective in the painful crisis of tabes. Cases with intense changes in the spinal fluid seem to react better than others. Complete failures are rare. The author has had good results in 15 out of 23 cases, moderately good in 6 and only 2 failures. Generally 2 to 3 series of irradiations are necessary. Three to four fields 10×15 cm. in size are irradiated with 30 cm. focus-skin distance, 0.5 mm. copper and 1 mm. aluminum filter, 180 kv., 40–50 per cent of a skin erythema dose per field. One field is

irradiated every other day until the whole cord has been covered. A second series is given after six to seven weeks and a third if necessary after three months. In gastric crises the solar plexus may also be irradiated with 20–25 per cent of a skin erythema dose. Tabetic arthropathies, like chronic and subchronic joint diseases in general, respond well to irradiation.

Roentgen treatment is also very effective in poliomyelitis, especially in recent cases. The treatment may be combined with diathermy, electrotherapy and injections of trypaflavin. A particularly striking case of cure is mentioned in a young girl with total paresis of both legs and severe disturbances of bladder and rectum. Good results have been obtained in chronic cases also but never complete cure. The whole spinal cord is irradiated in 4 fields in acute cases with 25–30 per cent of a skin erythema dose, in chronic ones with 50 per cent. If only the upper or lower extremities are affected only the lower or upper part of the cord is irradiated.

The results are not so good in encephalitis and acute epidemic meningitis, though in the latter disease the enormous overproduction of spinal fluid is sometimes decreased. Roentgen therapy is valuable in multiple sclerosis because there is no other effective method of treatment. Among 17 cases the author had excellent results in 12, considerable improvement in 4 and failure in only 1. This is better than the results reported by other authors and the author thinks this may be due to his technique. He generally gives only 20–25 per cent of a skin erythema dose per field, never more than 40 per cent. When the brain is involved he irradiates 2 brain fields 10×15 cm. in addition to the 4 spinal cord fields.

Among constitutional or general diseases of the central nervous system he has had good results in habitual headache of unknown etiology resistant to other treatments. On the basis of five years' experience he thinks roentgen irradiation the treatment of choice in these headaches. Roentgen therapy is also indicated in traumatic compression and serous meningitis.

In epilepsy in children cure is reported in 3 cases and considerable improvement lasting over two years in 2 others. In genuine epilepsy in adults 8 cases were cured, 11 improved and 5 were refractory. None were absolutely refractory. There was temporary improvement in all cases but in these 5 it lasted only a few weeks. Adults are given 50 per cent of a skin erythema dose per field and children 30 per cent.

The subjective improvement in syringomyelia is great enough to justify the use of roentgen treatment. Among the 3 cases the author has treated 2 were greatly improved at first but grew worse after six months and withdrew from treatment. He has had no personal experience with Raynaud's disease but good results have been reported. He has had good results in 4 cases of arteriosclerotic dysbasia with 60–70 per cent of a skin erythema dose, 2 series with an interval of six to eight weeks.

He has always had good results in sciatic and facial neuralgia. In sciatica he irradiates the lumbar and sacral cord and 4 to 5 fields along the sciatic nerve, in trifacial neuralgia the Gasserian ganglion and the trifacial nerve. He has had improvement in 7 cases of paralysis agitans from irradiating the region of the 4th ventricle with 20 per cent of a skin erythema dose, but complete cure in none.—*Audrey G. Morgan.*

Röhr, H. O. Die Röntgentherapie der chronischen Arthritiden. (The roentgen therapy of chronic arthritis.) *Strahlentherapie*, 1931, *42*, 425–436.

The author discusses the results of roentgen treatment of 40 cases of chronic arthritis. About half of them were primary or secondary chronic arthritis, the others arthritis deformans and a few cases of gout and septic and endocrine arthritis. Generally irradiation was given only after other treatment had failed.

Formerly he used doses of 40–50 per cent of a skin erythema dose but found that they were not any more effective than smaller doses and were more or less injurious to the bones and joints. He now uses not more than 20 to 30 per cent of a skin erythema dose with a tension of 180 kv., a filter of 0.5 mm. copper and 1 mm. aluminum, 4 ma. and a focus-skin distance of 30 cm. Large fields are used so as to irradiate not only the joints but the periarticular tissues. Three to four fields are used for the large joints and 2 for the small ones with an interval of 3 or 4 days between irradiations.

The pain began to decrease often the day after the first irradiation. The mobility of the joints also improved and effusions were absorbed. The improvement in motility was per-

manent though it was not brought about so quickly as cessation of pain. Young patients reacted better than old ones. The subjective symptoms were relieved in old cases as well as in fresh ones. In arthritis deformans crepitation was overcome and proliferations and even calcium deposits disappeared.

The mechanism of action of the rays in arthritis is not very thoroughly understood. They seem to have a specific anodyne action in rheumatic joint disease and also to destroy joint proliferations and stimulate the cells to normal function.—*Audrey G. Morgan.*

Corscaden, James A. Anatomic changes subsequent to the radiotherapeutic treatment of benign uterine conditions. *Am. J. Obst. & Gynec.*, July, 1931, *22*, 74–86.

The author analyses 434 cases with reference to the effect of irradiation on the size of the myomatous uterus; the importance of roentgen rays and radium as excitants of latent infections; the frequency and importance of subsequent changes within the tumor, such as degeneration and sarcoma; the occurrence of carcinoma of the body and neck of the uterus and disease of the tubes and ovaries, especially those conditions which were overlooked at the time the treatment was given and later became apparent.

In the literature considerable emphasis is placed upon the danger of exciting quiescent foci of infection by radium and roentgen rays. Many such cases are reported, but the precise lesion is less often described. Corscaden concluded that the cause of inflammation following the introduction of radium was due to an operative contamination rather than to some less obvious effect of the electromagnetic waves upon either the tissues or bacteria in a residual inflammatory focus. In fact, several cases in which there was definite inflammation showed improvement following roentgen therapy. Polak and Gál, who have had similar experiences, employ roentgen radiation as a therapeutic measure in the management of acute pelvic inflammatory disease.

In patients treated for uterine myomas, the growth was stopped in all patients treated, reduction has occurred to a satisfactory degree in 83 per cent, and there has been complete reduction of the mass to the size of a normal uterus in 55.2 per cent.

The author, basing his statement on the government mortality statistics, states that 2.4 per cent of women in general develop carcinoma of the uterus. Only 1.28 per cent of his cases treated for fibromyomas subsequently developed carcinoma of the uterus—observations having been over a period of seven years.

The evidence permits the author to conclude that the incidence of disease in the organs of reproduction after treatment by roentgen rays and radium is a little less than in women in general. The occurrence of uterine bleeding and discovery of a small myoma does not make the patient a candidate for promiscuous prophylactic excision; with the growth stopped and the uterus made smaller by roentgen rays or radium, she has the same chance for health as the women without these conditions.

The importance of a diagnostic curettage is emphasized. Corscaden encountered unexpected pathology (carcinoma of the body of the uterus, epithelioma of the cervix, pedunculated intrauterine myomas, polyp) in 3 per cent of his cases, causing a change in the method of treatment.—*J. H. Vastine.*

Gunsett, A. La Roentgentherapie du cancer de la vessie par la méthode de la dose fractionnée. (Roentgen therapy of cancer of the bladder by the method of fractional dosage.) *Acta radiol.*, 1932, *13*, 1–20.

The author reports 26 cases of cancer of the bladder treated from 1922 to 1929. All of these cases were treated by roentgen irradiation given in divided doses distributed over a period of about three weeks. In the first case treated in 1922 the dose was 128 per cent of an erythema dose given in five days. From 1924 on, the dosage was measured with Solomon's ionometer, from 4,000 to 5,000 R being given in three weeks with a filter of 1 mm. zinc or copper (later 2 mm. copper) and 2 mm. aluminum, focus-skin distance 40 cm. Some of the patients were given roentgen irradiation only, while in other cases the roentgen irradiation was preceded or followed by electrocoagulation.

Of the 26 patients 10 are still alive and free of symptoms at the beginning of 1932, one who was treated in 1922, one in 1923, two in 1924, two in 1925, one in 1926, one in 1928 and one in 1929; that is, among 19 cases there are 8, or 42 per cent, cured after five years' observation.

The author believes that the treatment of large bladder tumors should begin with deep roentgen therapy, and electrocoagulation should be used later to destroy any parts of the tumor that still remain after roentgen treatment.

Roentgen therapy may also be used after electrocoagulation that has given imperfect results. —*Audrey G. Morgan.*

Jacobs, A. W. Carcinoma of ovaries, with recurrence and metastases, treated by surgery and radiation. *J. Am. M. Ass.*, Jan. 23, 1932, *98*, 315.

A study of a series of cases of carcinoma of the ovary showed the average duration of life from diagnosis to death to be twelve months in cases not given roentgen therapy and twenty-three months where roentgen therapy was instituted. The belief is expressed that irradiation of the pelvis in cases of suspected carcinoma of the ovary followed in six weeks by surgical measures would give better results than the usual procedures. A case is reported in which a microscopic diagnosis of ovarian papillary adenocarcinoma was made. Surgery and roentgen therapy have kept the patient in comparative health and comfort for twelve and one-half years despite definite recurrence with tumor and ascites.—*E. W. Hall.*

Körbler, Juraj. Die Röntgenbehandlung des Peniskarzinoms. (Roentgen treatment of carcinoma of the penis.) *Strahlentherapie*, 1931, *42*, 780–783.

Two cases are described. The first was in a man of forty-three. The whole prepuce was involved in the tumor. The Wassermann reaction was negative. The inguinal glands on both sides were removed by operation and the patient irradiated with a dose of 15 H filtered through 0.5 mm. copper and 1 mm. aluminum, given over two fields and in 2 treatments with an interval of three weeks between. Three months after the irradiation the whole penis was soft but in the distal part of the prepuce there was a suspicious area. Circumcision was performed under local anesthesia; histological examination of the prepuce showed pavement cell carcinoma. On the basis of this finding amputation was advised and accepted, but the penis did not show any carcinoma tissue. The circumcision would probably have sufficed for permanent cure.

The second patient was a student of twenty-three who was irradiated in the same way for a tumor involving both the prepuce and the glands. The inguinal lymph glands were removed operatively and did not show any tumor tissue. Eight months after irradiation there was no trace of a tumor but there was pronounced phimosis. The prepuce was removed and did not show any tumor tissue.

The author advocates roentgen treatment for even operable tumors of the penis as it prevents loss of sexual power with its disturbing consequences and operation can be performed later if necessary. These tumors show little tendency to metastasis.—*Audrey G. Morgan.*

Kamniker, Hellmut. Behandlungsergebnisse und Dauerheilungen beim Collumcarcinom. (Results of treatment and permanent cures in carcinoma of the cervix.) *Arch. f. Gynäk.*, 1932, *148*, 12–30.

At the University Gynecological Clinic in Vienna 522 cases of carcinoma of the cervix were treated from 1921–25 and 471 from 1926–1930, making a total of 993. The five-year results are known only in the first group of cases. The cases are divided into four groups according to the severity of the disease. There were 97 cases in Group I, 188 in Group II, 181 in Group III and 56 in Group IV. Among these cases 304 were operated on or an attempt made at operation, 191 were irradiated, 6 refused any treatment and 21 were in such desperate condition that no treatment was attempted. The percentage of operability was 58.2. Of the cases operated on 88 were in Group I, 162 in Group II, 41 in Group III and 13 in Group IV. In some of the latter group the operation could not be finished on account of technical difficulties. These cases would not now be considered operable but would be irradiated. The primary mortality in the Group IV cases was 50 per cent. The primary mortality in all the groups taken together was 6.3 per cent and in Groups I, II and III only 4.8 per cent. Among the operated cases 236 were operated on by radical vaginal extirpation. Of these, 114 are alive and free of recurrence after five years, or 48.3 per cent. In Group I there was 61.9 per cent five-year cures, in Group II, 43.8 per cent, in Group III, 48 per cent, while in Group IV all the patients died. Comparing the cases treated by surgery alone with those in which surgery was followed by irradiation, there were five-year cures in 46.5 per cent of the former group and in 64.2 per cent of the latter, showing that the results are improved by about 18 per cent by postoperative irradiation.

Among the 191 cases treated by irradiation alone only 8 were cured, or 4.2 per cent. It is true that the majority of these were in Groups III and IV and the prospects for cure were not

good. It is also true that the technique was not so well developed at that time as it is now and that with the technique now in use there would probably have been 10–15 per cent cures even in this unfavorable material.

The author concludes, however, that operable cases of cancer of the cervix should still be operated on. Statistics are cited from the clinics of Munich, Paris, Stockholm and Vienna which show that operation in Group I gives 18 per cent better results than irradiation and in Group II the results of surgery are still better than those of irradiation. But in Groups III and IV irradiation gives better results than surgery. And in all groups surgery with postoperative irradiation gives better results than surgery alone.—*Audrey G. Morgan.*

Muhlmann, E. Ergebnisse der Strahlenbehandlung des inoperablen Kollumkarzinoms 1920–1927. (Results of radiation therapy of inoperable carcinoma of the cervix from 1920 to 1927.) *Strahlentherapie*, 1931, *42*, 504–509.

The results of the roentgen division of the Municipal Hospital of Stettin are reported. From 1920 to 1927, 237 cases of inoperable carcinoma of the cervix were treated with combined radium and roentgen irradiation. The roentgen irradiation was given in the form of a single large dose of 100–110 per cent of a skin erythema dose. Among these cases 46, or 19.74 per cent, were cured and have remained well for more than five years. From 1915 to 1918, 30 cases were treated with radium alone and 16.6 per cent of these were cured and have remained so for more than five years. The author concludes from this that combined therapy is not superior to radium alone, at least in the form in which they have used. it. He intends trying the protracted method of Coutard which may give better results.—*Audrey G. Morgan.*

Martius, H. Die Behandlung der weiblichen Genital tuberkulose. (Treatment of genital tuberculosis in women.) *Strahlentherapie*, 1931, *42*, 471–484.

Cases of genital tuberculosis in which there is a progressive lung process or tuberculosis of the intestines, bones or kidneys should not be operated on but should be given roentgen treatment. Irradiation has given good results not only in these cases but also in those in which operation has been incomplete. Many cases of genital tuberculosis, however, cannot be diagnosed without exploratory operation. The author found this true in 10 out of 28 cases.

The introduction of roentgen treatment has modified the nature of the operation in genital tuberculosis. It is not now necessary to operate so radically, as operation can be supplemented by irradiation and the operation has therefore become less dangerous. This is particularly true when there are extensive intestinal adhesions. Only tissue should be removed by operation that can be reached readily and that is not firmly adherent. If there is no pathological hemorrhage the uterus need not be removed if it is normal macroscopically and the ovaries may also be left in place in young women if there are no macroscopic changes in them.

Except in cases in which operation is required for diagnosis the author believes primary irradiation is to be preferred to operation as the operative morality is about 10 per cent. At the Bonn Clinic 9 cases have been treated by primary irradiation. One young girl died six months later of pulmonary tuberculosis after marked improvement in the genital disease. Four of the 8 remaining cases are completely cured and 4 greatly improved. In the older literature only the worst cases were given primary irradiation. In cases with ascites the author recommends incision for evacuation of the fluid with no further operation, followed by irradiation. The 71 cases treated at the Bonn Clinic from 1917 to 1930 are divided into 2 groups, the first from 1917 to 1923 before this method of treatment was adopted and the second from 1924 to 1930 after it was adopted. The mortality in the former group was ten times as great as in the latter.

Roentgen dosage should be small in genital tuberculosis as the object is not to destroy the diseased tissue but to stimulate the defensive forces of the body. One large field on the lower part of the body is irradiated with a focus-skin distance of 50 cm. This field is given a dose of 110 r, about a third of the skin tolerance dose of 590 r. This irradiation is repeated 3 times with intervals of a week. The further treatment depends on the clinical course. This is less than the ovarian dose. The author does not believe ovarian function should be abolished. The roentgen treatment should be supplemented by the usual treatment for tuberculosis, such as good food, sunshine, etc.—*Audrey G. Morgan.*

Gilbert, R., and Babaiantz, L. Notre methode de roentgenthérapie de la lymphogranulomatose (Hodgkin): résultats éloignés. (Late

results of our method of roentgen therapy of Hodgkin's lymphogranulomatosis.) *Acta radiol.*, 1931, *12*, 523–529.

The authors advocate giving a large enough dose of radiation to destroy the granulomatous lesions with the first series. They concentrate the rays first on regions that can be shown clinically to be affected and then, if the patient is able to stand it, as shown by the blood picture, extend the irradiation to regions that are apparently normal but which experience has shown are frequently affected by the disease. A diagram is given showing the fields of irradiation in a cervical and mediastinal form of lymphogranulomatosis. They use a tension of 180 to 200 kv., an intensity of 2 to 4 ma., a filtration of 0.5 to 1 mm. copper and 1 mm. aluminum and focal distances which vary with the depth of the focus and the size of the fields to be irradiated. The total depth dose in the majority of cases is 400 r for the first series of irradiations. The total incident dose in relatively superficial adenopathies, such as those of the cervical and axillary glands, is from 700–1,100 r, depending on the size of the adenopathy, generally from one field. For mediastinal tumors about 4,000 r is given from 4 large fields, or about 1,000 r per field. Of course the dosage must be individualized; larger doses may be given in sclerotic cases. As a general rule 170 r is given at one sitting once a day or every other day; the dosage is extended over ten to fifteen days for each field with a total duration of the treatment of four or five weeks. Arsenic and general tonic treatment are generally given also. A vegetarian diet seems to be particularly valuable in this class of cases.

The authors report their late results with this method after an observation time of nine years. Among the 15 cases treated, 7 patients were still alive at the end of April, 1931, representing at that time an average survival of six years from the beginning of treatment. One of these 7 has since died. The remaining 6 cases still represent an average survival of four years and three months.—*Audrey G. Morgan.*

Santoro, Angelo. L'Attivita della Sezione radiumterapica nel triennio 1928–1931. (Work of the radium therapeutic section for the three years 1928–1931.) *Arch. di radiol.*, 1931, *7*, 1113–1125.

The author discusses the results for the past three years in the radium therapeutic section of the Institute of Medical Radiology of the Royal University of Rome. The article is devoted chiefly to results. Reference is made to previous articles for details of technique, the author merely stating that their rule is to reach the saturation point of the diseased tissue slowly. So far as possible tumors are treated with a single dose, keeping the preparation on for several days until the maximum dose has been given.

Within the three years they have treated 40 skin cancers of the face with cure in 26, one disseminated skin cancer of the back with the patient improved and living, 6 cancers of the genitourinary organs with cure in all, and 16 cancers of the cervix. Eight of these had had no previous treatment and 6 were cured. Eight were treated for operative recurrence and 2 cured. There were 9 cases of cancer of the breast, 5 of which were cured. There were 36 cases of cancer of the digestive tract including 6 of the lips, all of them cured, 6 of the cheek with 2 cures, 7 of the floor of the mouth with 3 cures, 7 of the tongue with 3 cures, 6 of the pharynx with 3 cures, 1 of the hard palate, result as yet unknown, 1 of buccal leucoplakia cured and 2 of cancer of the esophagus improved. In 3 cases of cancer of the rectum there was improvement which amounted to apparent cure in 2. Among cancers of the respiratory tract there were 4 of the larynx with cure in 2 and improvement in 2, three of papilloma of the nose with cure in all, 2 metastatic tumors of the lung with disappearance of the shadow in 1 and the patient in good general condition two months later, and 2 fibromas of the nasopharynx, both cured. Among sarcomas there were 5 of bone with 4 improvements and 1 cure, and 3 of muscle, all improved. One tumor of the parotid gland was cured. Among 7 craniopharyngeal tumors 1 was cured and 6 improved, and among 3 tumors of the brain 1 of the hypophysis was cured. Among 20 cases of lupus 10 were cured; among 65 angiomata 60 were cured; among 10 keloids 7 were cured. Two cases of rhinophyma were cured and 2 cases of neuralgia resistant to all other treatment have remained cured for a year and a half.—*Audrey G. Morgan.*

Holfelder, Hans. Methodische Fortschritte der Röntgentherapie der Krebse des Verdauungskanals. (Improved method of roentgen therapy of cancer of the digestive tract.) *Strahlentherapie*, 1931, *42*, 497–503.

With former methods of treatment irradia-

tion of the digestive tract, especially the stomach region, has caused such severe roentgen sickness that irradiation of these tumors almost had to be abandoned. The author describes a technique by the use of which he has had good results without unpleasant by-effects.

The principle of the method is the use of small fields 6×8 cm. in size. The skin is sharply compressed with a curved tube. In carcinoma of the stomach 4 to 8 different fields can be used, a position being chosen such that the carcinoma lies in the first part of the cone of rays. On the first day, 2 to 3 fields are irradiated, on the second day 2 fields and then one field a day for four to six weeks. The dose for each field each time is 300 r measured in air; the total dose per field is 2,400 to 3,000 r. But this amount can be borne without injury only if the skin is sharply compressed. The method is very similar for carcinomas of the rectum. Two cases are described and illustrated with roentgenograms.—*Audrey G. Morgan.*

Dieterich, W., and Umbach, J. Unsere Erfahrungen mit der protrahiert-fraktionierten Bestrahlungsmethode. (Experience with the protracted fractional method of irradiation.) *Strahlentherapie*, 1931, *42*, 510–513.

The authors tried irradiating malignant tumors of different organs by the protracted fractional heavy filter method. The technique was as follows: focus-skin distance 40 cm., size of fields 10×15 cm., tension 219 kv. maximum, 4 ma., 3.0 mm. zinc, half-value layer 2.1 mm. copper. The skin erythema dose was assumed to be 550 r. Each field was irradiated with 185 r at a time and this dose repeated daily until 3,000 r had been given to the chief field and 1,200 r to the auxiliary fields. The treatment extended over a period of four weeks. Several inoperable stomach carcinomas in which the diagnosis had been confirmed by exploratory excision were treated in this way and there was very great objective improvement in all of them. The tumors disappeared and only some rigidity of the curvatures could be seen in the roentgenogram.

To compare the value of hard and medium rays one patient with inoperable carcinoma of the stomach was irradiated with the same technique except that a filter of 0.5 mm. zinc and 1 mm. aluminum was used instead of 3 mm. zinc; each of the fields was given 1,600 r within a month without any injury to the skin. The tumor disappeared almost completely but it has not yet been three years since the treatment was given so the patient cannot be pronounced cured.

The author thinks the value of the method lies in the long time over which the treatment is extended, not in the hardness of the rays. Some forms of tumor respond better to very hard rays, some to moderately hard ones. But with the long period of treatment more carcinoma cells come under the action of the rays while they are undergoing division and so more of them are destroyed. The normal tissues are beginning to recover when the succeeding treatment is given while the tumor cells are still suffering from the irradiation and there is a cumulative action.

However, the method has not yet been in use long enough to be certain that there will be no late injury of the skin, so the authors believe the method should only be used for certain kinds of tumors.—*Audrey G. Morgan.*

Groedel, F. M., and Lossen, Heinz. Sur Frage der Röntgentotalbestrahlung. (The question of total roentgen irradiation.) *Strahlentherapie*, 1931, *42*, 532–538.

Roentgen irradiation of the whole body has been proposed for blood diseases and certain skin diseases and also for carcinoma. Teschendorf objected to this method, however, on the ground that amounts of irradiation would have to be given that could not be borne. The authors report a case which confirms this opinion. A man of sixty-one was treated for psoriasis of the whole body in the autumn of 1928. All the irradiations were given at a tangent to the surface of the body except in those regions where this was impossible. Tables are given showing the distribution of the irradiation over the different fields. A total of 1,830 per cent of a skin erythema dose was given over 37 fields. No examination of the blood was made during the whole time of the irradiation. Soon after the last irradiation in April of the next year the patient became very anemic. A typical aplastic anemia developed which was treated unsuccessfully with blood transfusion and liver and arsenic therapy. The patient finally recovered after extirpation of the spleen. The psoriasis was cured.

Such total irradiations should not be called roentgen baths, as they sometimes are, for a bath affects only the surface of the body and in any kind of roentgen treatment the deep effect must be reckoned with.—*Audrey G. Morgan.*

Pfahler, George E. The roentgen-rays and radium in the diagnosis and treatment of carcinoma of the bladder. *Surg., Gynec. & Obst.*, Nov., 1931, *53*, 680–690.

Pneumocystography, which was described first by Pfahler in 1910 and has been employed by him since, is discussed. The technique is described and the following advantages enumerated: (1) safety of the procedure—no untoward effects following several hundred pneumocystograms; (2) the exact size, position and outline of the bladder can be outlined which would at least be partially covered by an opaque medium; (3) the degree of infiltration of the bladder wall can be determined roughly by the flexibility or distensibility of the bladder wall.

Treatment of Bladder Tumors. Irradiation may be applied in various ways, but no methods have yet produced enough cures to make one enthusiastic or satisfied. This dissatisfaction also applies to surgical excision. Lower reported a five-year surgical cure in 7 per cent of his cases, with a primary operative mortality of 9.8 per cent. Schall reports an operative mortality of 12 per cent in the papillary cases and 20 per cent in the infiltrating carcinoma. It must be remembered that these are operable cases while the cases treated by irradiation are usually advanced and inoperable.

The radiation methods of treatment may be any of the following: (1) Unscreened radium may be applied directly in small tumors and tumors about the neck of the bladder, the radium being held in direct contact through a cystoscope as recommended by Barringer. (2) Seeds either of glass, or better, gold, may be implanted directly into the base of the tumor, cystoscopically or suprapubically as recommended by Barringer, Keyes, Hyman, Burman, Marson, and others, but is suitable only for small tumors. (3) The disease may be excised and then treated by deep roentgen therapy. (4) The disease may be destroyed by electrocoagulation and then treated by the implantation of removable radium needles as has been used by Pfahler for a time, only in very large and inoperable tumors, through a suprapubic cystotomy but which method has now been abandoned (Thomas and Pfahler, MacKenzie, and others). (5) Through a suprapubic cystotomy the prominent tumor may be snared away and the base implanted with radium seeds (Barringer). (6) Deep roentgen therapy may be used upon the primary tumor as has been recommended by Waters, Gunsett, Schmitz, Schnoebelin, and others, and which method seems to the author to be most satisfactory. It is to be recommended especially in the inoperable tumors, and preliminary to operation.

The results of various authors are discussed. Smith reported 27, 27, and 29 per cent of the cases symptom-free in two years following excision, electrocoagulation and radium treatments respectively. Barringer reported 43 per cent of three-year recoveries in papillary carcinoma and 29.7 per cent in the infiltrating type. Waters recommends surgery when operable, otherwise roentgen therapy plus surface applications of radium to the tumor. Grier reported 3 recoveries following roentgen therapy in 17 inoperable cases. Burman reported 9.9 per cent cures in the large inoperable carcinomata and 35 per cent cures in smaller lesions. Pfahler's results—based on 83 advanced inoperable cases of carcinoma of the bladder—are as follows:

Of 43 cases treated by suprapubic cystotomy, electrocoagulation and radium needles there was a 15.6 per cent five-year survival.

Of 7 cases treated by surgical excision and postoperative roentgen treatments all died.

Of 6 cases treated by surgical excision followed by radium packs in bladder against base all died.

Of 5 cases treated by surgical excision, radium packs in bladder and roentgen therapy, 2 were symptom-free one year and another seven months after treatment.

Of 8 cases treated by electrocoagulation, cystoscopically followed by roentgen and radium treatment, 3 were symptom-free seven, five and two and a half years later.

Of 12 cases treated by irradiation only, there were 4 symptom-free fifteen, three and one-half and one year and seven months after treatment.

The author feels encouraged with the treatment by irradiation particularly combined with electrocoagulation, cystoscopically in the early cases and radium tampon in the vagina in selected cases. Many of the above cases were treated with the "low voltage" technique which may tend to lower the statistical results. The author emphasizes the value of irradiation as a palliative measure in cases which cannot be cured.—*J. H. Vastine.*

Moench, L. Mary. Primary epithelioma of the vagina. *Am. J. Obst. & Gynec.*, Dec., 1931, *22*, 837–851.

Primary carcinoma of the vagina constitutes less than 1 per cent of all carcinomas in women. In the Mayo Clinic, between 1915 and 1925, there were 29 cases of carcinoma of the vagina seen, the ratio being one primary vaginal carcinoma to every 43 of cervical carcinoma.

Two forms of early lesion occur. One of them simulates a benign papilloma so closely that microscopic examination must be depended on for diagnosis. A single papilloma with an indurated base should be considered as possibly malignant, until it is proved otherwise by biopsy. A soft, proliferating, friable mass develops as a later stage of the growth and is more easily recognized clinically as being malignant. The second form of the initial lesion, in an early stage, may appear as a small, firm nodule, which in a later stage breaks down into an ulcer, with a characteristically firm margin, suggesting in some respects a syphilitic lesion. If the dark-field examination is negative, biopsy should be performed. Although the early lesion often appears clinically insignificant, microscopic study reveals the growth to consist, in the majority of cases, of an undifferentiated, rapidly growing type of ce'l, of malignancy graded 4 by Broders' method, a classification which is further substantiated by the rapidly progressive clinical course of the disease.

The highly undifferentiated type of cell which is characteristic of the majority of these growths is not the only important cause for the rapid course of this disease. The vagina is richly supplied with lymph channels, and fairly early metastasis to the regional lymph nodes occurs. Metastasis is to the inguinal nodes if the lesion lies in the lower third of the vagina; to the middle chain of the external iliac group of lymph nodes, to the hypogastric group, and to the nodes which lie over the promontory of the sacrum if the primary growth lies in the superior two-thirds of the vagina.

The author analyzed 59 cases from which specimens had been obtained for biopsy in 37. Of these, 35 were squamous cell epitheliomas, and 2 were adenocarcinomas. They were of a high grade of malignancy, 20 being grade 4 (Broders'); 12, grade 3; 2, grade 2 and 1, grade 1.

Sixty-five per cent were on the posterior vaginal wall; 17.5 per cent were on the anterior vaginal wall; 7.5 per cent were on the lateral walls and 10 per cent were so extensive that their primary sites were uncertain. The large majority of the women were married and 83 per cent of the married women had borne children, the average number of children being three.

The average age incidence was forty-nine years, the youngest patient being twenty-eight years of age.

Results. Of the patients treated by irradiation only, the average duration of life was 34.5 months, while of those treated by surgery and irradiation (all early cases) the average duration of life was only twelve months. This, the author feels, shows the definite palliative value of irradiation. *Radiotherapy has resulted in arrest or cure in 6 of 12 early cases (50 per cent) as opposed to 2 of 12 cases (16.6 per cent) treated by operation only.* Radiotherapy also has resulted in arrest or cure in one case of 21 advanced cases; this case would have been rejected for operation only, because of pelvic glandular involvement. By all methods of treatment, however, only 9 patients of 53 concerning whom the results were known have survived without evidence of recurrence for from two to twelve years, a percentage of so-called cure of only 17 per cent.—*J. H. Vastine.*

Lynch, Frank W. A five to fifteen year follow-up study of one hundred ninety-two cervical cancers. *Am. J. Obst. & Gynec.*, Oct., 1931, *22*, 550–558.

Treatment of Groups I and II consisted of preoperative irradiation, operation by a modified Ries technique, and followed by postoperative irradiation in some cases. There was a 67.8 per cent five-year salvage in 31 cases. Of 3 patients in Group I who were treated by irradiation alone, all, or 100 per cent, lived over five years. Nine cases in Group II were treated by irradiation of which 6 died from carcinoma, 2 of intercurrent disease, 1 survived five years.

Groups III and IV comprised 113 cases, treated by radium alone or rarely by radium and deep roentgen rays; 7.1 per cent of the cases in these two groups survived five years.

Group V, the postoperative recurrences, comprised 43 cases, of which 4, or 12.1 per cent, were cured five years. All of these were treated only by irradiation.

The striking point of this report is the good results, 67.8 per cent five-year cures, obtained by combined preoperative irradiation, a very radical type of Wertheim operation and occasional postoperative irradiation. The operative mortality was 12.9 per cent showing the operative procedure to be rather extensive, probably too radical for a less heroic surgeon.

The author does not attempt to evaluate the relative merits of irradiation and surgery but he does state that the results of radium, even in operable cases, far surpass those of ordinary panhysterectomy even in cases deemed sufficiently operable to warrant operation.—*J. H. Vastine.*

Ward, George G., and Farrar, Lilian K. P. Reradiations in the radium therapy of carcinoma of the cervix uteri. *Am. J. Obs. & Gynec.*, Oct., 1931, *22*, 543–550.

Radium does not remove a cancerous growth by destruction of the entire part affected, as is accomplished by surgery or cautery, but the gamma rays have a direct selective action on the cancer cells, destroying them without injuring the normal cells around the site of the neoplasm. Underdosage will fail to destroy the cancerous growth while overirradiation will produce a destruction of the normal structures beyond repair and produce extensive necrosis with resulting septic absorption, hemorrhages, and injury of adjacent viscera, with perhaps the formation of fistulas. Therefore, it is not generally regarded as sound technique by most authorities to expose carcinomatous tissue to repeated irradiations over long periods of time. Schmitz states that following the initial treatment should healing of the cancer not ensue, it is not advisable to repeat the treatment. Regaud, Nogier, Delbet, Mocquot, Herrenschmidt, and others, have stated that cancer cells develop a radioresistance after repeated dosage. In accordance with this view which generally prevails, the technique usually in vogue is to complete the treatment in a relatively short time, and should recurrences appear, to regard further radiotherapy as harmful and useless.

The technique employed at the Woman's Hospital consists in the employment of the indicated measures for building up the patient's general health and the employment of a test dose of radium varying from 2,400 to 4,200 mg-hr. The patient is observed carefully and frequently, and further irradiation is given at the earliest sign of recurrences. Re-irradiation is necessary in nearly 50 per cent of the cases. This is usually employed for metastases in the vaginal walls or fornices, and is usually administered interstitially in the form of 12 mg. platinum needles, although surface applications are occasionally employed. The average dosage ranges from 300 to 1,200 mg-hr. in these re-irradiation cases. In regard to re-irradiation, Heyman advises interstitial irradiation with radium needles in cases of persistent small residua and in the cases of small vaginal recurrences. Taussig has advised re-irradiation as being of value. The standard treatment at the Munich Clinic is to administer a second irradiation eight, and if necessary again sixteen weeks after the initial treatment.

Ward and Farrar analyzed 147 cases in which re-irradiation was necessary in 75 cases. Of these 75 re-irradiated patients, 24 per cent lived five years or longer.

Adenocarcinoma of the cervix is usually regarded as very radioresistant. Regaud states that he has had very few cures in this type and advises operation. This is contrary to the authors' experience in which 30.7 per cent of their cases with adenocarcinoma lived five years or longer.

Ward and Farrar found the three-year cures can be regarded as an index of the value of irradiation as a therapeutic measure in carcinoma of the cervix since between three and five years the difference was only 8.7 per cent, the normal mortality rate for two years at the average age of fifty.—*J. H. Vastine.*

Crossen, H. S. Conclusions from a study of five-year cures in a series of 121 cases of carcinoma of the cervix uteri. *Am. J. Obst. & Gynec.*, Oct., 1931, *22*, 559–570.

At the Barnes Hospital of the Washington University Medical School, radium and roentgen rays have been employed in the treatment of carcinoma of the cervix for the past ten years.

Group I comprised 2 cases treated by operation alone both of which have survived five years.

Group II comprised one case treated by preoperative radium therapy, operation and postoperative radium therapy. This case has survived over five years.

Group III (extensive involvement of parametrium with fixation of uterus to the pelvic wall) comprised 108 cases treated by irradiation alone, with 24, or 22.2 per cent, five-year survivals.

Group IV comprising 10 cases treated by irradiation alone contained no five-year cures.

In regard to irradiation, the author states that it is a powerful remedy which requires experienced judgment and skill in its use. It is as potent as the knife and in inexperienced hands may produce as disastrous results, either in the

form of injury to adjacent organs or failure to obtain results that might have been obtained by a really efficient application.

The author recommends giving the maximum dose at the first application. This is shown by a 35 per cent five-year cure in 17 patients receiving 5,000 mg-hr. at the first application, while there was only an 18 per cent cure in 79 patients receiving smaller initial doses. All of these patients were in Group III.

Deep roentgen therapy is considered essential as a post-radium or postoperative measure. Its value is illustrated by a case of advanced carcinoma of the cervix which was apparently cured by roentgen therapy alone, ultimately dying six years later from pneumonia.

The author avoids the depressing effect of general anesthesia, preferring introduction of radium under hyoscine-morphine sleep.—*J. H. Vastine.*

Meaker, Samuel R. Leiomyosarcoma of the uterus, with a report of four personal cases. *Am. J. Obst. & Gynec.*, Sept., 1931, *22*, 400–408.

Myosarcoma of the uterus is an exceedingly uncommon cause of death. Ewing states that in twenty years he has encountered only 3 cases of malignant uterine myomas with general metastases. The average of reports indicates that about 1 per cent of supposed leiomyomas will show histologic malignancy, many of these tumors which show a considerable degree of histologic malignancy are clinically benign. Only when the malignancy rises above a certain threshold does the growth burst its bounds and become an actual menace to life. Every leiomyosarcoma must be regarded and treated as a potentially dangerous neoplasm, even though it be well understood that the majority of such tumors are in fact relatively harmless.

Diagnosis. The symptoms and signs of this tumor are practically identical with those produced by benign leiomyoma. Rapidity of growth is probably the most informative single datum; while slow-growing tumors may or may not be malignant, those that grow rapidly are always worthy of suspicion.

Treatment. Good results in the treatment of uterine leiomyosarcoma have been obtained by irradiation alone, according to reports from certain European clinics. It would appear, however, that the most satisfactory treatment is radical operation, panhysterectomy with bilateral salpingo-oophorectomy, followed by deep roentgen therapy. When a supracervical hysterectomy has been performed on a mistaken diagnosis of leiomyoma, there should be a radium insertion in the cervical canal in addition to deep roentgen therapy.—*J. H. Vastine.*

Holthusen, H. Zur Geschichte der Langzeitbestrahlung. (History of "long-time" irradiation.) *Strahlentherapie*, 1931, *41*, 435–449.

Even early in the roentgen era, before it was possible to measure dosage, there were two different conceptions of the way in which rays should be applied. Freund advocated giving repeated small doses and Holzknecht giving a single dose as large as could be borne. Seitz and Wintz, too, believed that carcinoma tissue should be destroyed at once with a single large dose. But it was found that this caused a very severe general reaction and sometimes led to the development of roentgen cachexia. For a long time it was believed that better results could be obtained by increasing the hardness of the rays, making them more like the short-wave gamma rays of radium. But experimental research did not show that, for roentgen rays at least, the quality of the action was dependent on wave length.

Coutard of the Radium Institute, Paris, has worked out a method of protracted fractional dosage and has shown that the time distribution of the dose has an effect on the action of the total dosage. A certain dosage does not produce a fixed and constant action, but its effect is partly dependent on the way in which the dosage is distributed. With his long-continued and divided dosage a much larger total dose can be given without injury than by any former method. Other workers have applied the different principles of his method but none have combined them to form a whole as effective as his method. The work of his predecessors is reviewed. Coutard finds that the difference in radiosensitiveness between carcinoma tissue and normal tissue can be increased by the use of fractional doses. With his method the action of roentgen rays can be made to approximate that of radium and an actual qualitative change in the reaction of the tissues to the irradiation is brought about. He reports clinical results extending over a long period of time which show the superiority of his method at least in certain forms of carcinoma, particularly cancers of the upper respiratory tract. Jüngling in 1923 reported that carcinoma of the larynx could not be treated with roentgen rays because the

necessary dosage could not be given without injury of the surrounding tissues. The fact that Coutard's results are particularly good in such cases shows the superiority of his method. It makes it possible to give effective irradiation without danger of late injury.

The time rhythm is the essential thing in Coutard's method, particularly the considerable lengthening of the total irradiation time. Schinz calls the method "protracted fractional irradiation" but for the sake of a simpler name that emphasizes the most essential point the author proposes calling it the "long-time method."—*Audrey G. Morgan.*

Schroder, R. Über die ersten Erfahrungen mit der nach Coutard geübten Intensiv-Röntgenbehandlung bei weiblichen Genitalkarzinomen. (First experience with Coutard's intensive roentgen treatment in female genital carcinoma.) *Strahlentherapie*, 1931, *41*, 67–72.

Since June, 1930, the author has used Coutard's intensive treatment in 40 cases, with slight modifications to adapt its use to the pelvis. In one group of cases he used 180 kv., 2.3 mm. copper filter, 4 ma., half-value layer of 2 mm. copper. This gave 5–6 R per minute, so that 200 R was given in 33–38 minutes. The skin distance was 50 cm. and the size of the fields 10×15 cm. In another group of cases he used 170 kv., 1.5 mm. copper filter, half-value layer of 1.5 mm. copper. With a distance of 50 cm. a dose of about 4.5R was given per minute, with a distance of 70 cm. 2.5R per minute. The shorter distance and therefore shorter time was chosen in some cases because 1½ hours' irradiation, particularly in the abdominal position, was too hard on the patients. The longer distances and longer irradiation times were better borne than the shorter distances and shorter periods. The longer irradiations were generally used on the abdominal fields, the shorter ones on the back. Generally one or two fields were used in front and two in the back. One field was irradiated a day with a dose of 200 R measured in air. In this way each field was irradiated once in every three or four days. The series was generally repeated ten times, so that in 30 or 40 days each field was given 2,000 R.

This treatment was used in cases in which recurrence had taken place after operation or radium treatment in places not accessible to further operation or radium treatment; advanced cases in which radium treatment had been given and infiltrations had developed beyond the reach of radium; advanced cases that had not been given radium treatment and for after-treatment of operated or radium-treated cases without demonstrable recurrence.

Patients who were not in too advanced a condition of cachexia bore the treatment well. In general the effects were good. At least there were no bad or toxic effects from the intensive treatment. In some of the very advanced cases diffuse dissemination of the carcinoma took place not only in the bones but in parenchymatous organs. In later cases when a toxic effect was observed the treatments were given farther apart or stopped altogether.

The skin did not show any ulcers or necroses. The subcutaneous tissue was perhaps a little harder in the irradiated regions than elsewhere but did not show any other disturbances. The bladder and rectum were always emptied before irradiation. There was some tenesmus of the bladder and rectum after irradiation and in some cases redness and edema of the bladder mucous membrane, but no serious disturbances. During and after the treatment there was often considerable pain in the carcinomatous foci. Infiltrations the size of walnuts to the size of hens' eggs disappeared and the effect on the regional lymph glands was good. Large infiltrations in the pelvis and omentum receded and became harder and more localized. If there is too rapid destruction of carcinoma tissue abscesses may form which have to be opened surgically, but generally the broken down tissue is absorbed.

From his experience this far the author thinks he is justified in continuing the treatment and even in increasing the doses.—*Audrey G. Morgan.*

Bru, Camille. La radiothérapie dans les insuffisances ou les arrêts de la menstruation (chez la femme jeune). (Radiotherapy in the insufficiencies or arrests of menstruation—in the young woman.) *Bull. et mém. Soc. de radiol. méd. de France*, March, 1931, *19*, 131–136.

Since the beginning of 1924, the author has used roentgen therapy to stimulate the ovarian cells on the basis of the following experiences: (1) the growth of a tumor is always hastened by an insufficient dose of roentgen rays and (2) roentgen therapy for hemorrhagic fibromas, as a rule, leads to more abundant menorrhagias after two or three seances.

The following technique was employed: Suprapubic irradiation through two circular fields

of 9 cm. diameter, corresponding to the ovaries, 5 mm. Al filter, 29 to 30 cm. skin target distance, 200 to 250 R (Solomon) on the surface of the skin; three seances, given at 28-day intervals, as a rule eight days before the normal menstrual period.

The procedure was applied in a number of cases, 10 of which are briefly described in the text.

The conclusion is reached that the application of small doses of roentgen rays constitutes an advantageous means of regulating menstruation, which no doubt is considerably superior to all methods of opotherapy used at present.—*T. Leucutia.*

Delherm, Louis. Considérations sur le traitement de la poliomyélite. (Considerations on the treatment of poliomyelitis.) *J. de radiol. et d'électrol.*, July, 1931, *15*, 321–326.

The methods of treatment of acute poliomyelitis may be divided into three groups: (1) The pathogenic treatment: roentgen therapy; voltaic current, with or without ionization. Roentgen therapy is of value especially in the beginning of the disease before a total reaction of degeneration of the muscles has set in. Generally, the sooner the treatment is instituted, the greater the chances for an improvement or cure. The same applies to the ascending or posterior anterior voltaization and to the diathermy and ionization as proposed by Bourguignon. All these procedures aim to act on the cells which have not as yet been destroyed preventing the formation of sclerotic tissue. (2) Treatment of tissue nutrition of the affected extremity. For this purpose local balneation, light and infra-red baths, etc., are recommended. (3) Excito-motor treatment of the muscle. The alternative long period galvanic waves of Laquerrière, eventually associated with ultraviolet radiation and in the later stages with massages, have a very beneficial action on the tonicity of the muscles.

Certain pediatricians have affirmed that roentgen therapy has "revolutionized" the prognosis of infantile paralysis. Although this statement appears too bold, good results are obtained nevertheless in a great number of cases.—*T. Leucutia.*

Grashey, R. Allgemeine Neben- und Nachwirkungen der Röntgenstrahlen. (General by- and after-effects of roentgen irradiation.) *Strahlentherapie*, 1931, *41*, 39–46.

Some of the general by-effects and after-effects of roentgen irradiation are indirect distant actions on the circulatory or nervous systems while some are due to irradiation of tissues which should not have been exposed to the rays. The most striking sign of general action of the rays is what is called roentgen sickness. It is an intoxication that is by no means specific and generally transitory. It is caused by products of catabolism of the irradiated cells entering the circulation. It is particularly intense when very sensitive tissue is acted on, such as lymphatic tissue or large sarcomas. Nervous predisposition also increases intensity of roentgen sickness.

Roentgen sickness is accompanied by changes in the blood picture, in basal and mineral metabolism and in the cholesterin and sugar content of the blood. There is an immediate fall of leucocytes. The erythrocytes are much more resistant. Most individuals quickly recover, but if the patient has been in poor condition or the irradiation has been too intense roentgen cachexia may develop. Blood examination should be made before every irradiation in order to keep the change within bounds.

After-effects from irradiating tissue that should not be irradiated can generally be prevented by carefully covering the tissues outside the zone to be irradiated. Holzknecht considers the fever and fine skin exanthems that occasionally occur toxemic in origin. Politzer thinks the asthmatic symptoms sometimes seen after irradiation of the spleen in leucemia are anaphylactic, though bronchial asthma is sometimes favorably affected by irradiation of the spleen. These distant actions are very puzzling.

The radiosensitiveness of the different organs varies greatly. The blood-forming organs are particularly sensitive, while irradiation of the circulating blood is less serious. Reproductive tissue is so sensitive that great care must be exercised in repeated irradiation of the pelvis, even for diagnostic purposes. The normal liver is moderately radiosensitive. If it is diseased or even temporarily injured by general anesthesia it is very sensitive. The kidney vessels are injured by large doses and also the pancreas and the mucous glands of the stomach. The normal thyroid is not particularly sensitive but in hyperthyroidism small doses should be given, particularly in the beginning. The brain, eye and ear, heart muscle, larynx, bladder and intestine are injured by large doses. Care should be used in irradiating children, as excessive irradiation may cause disturbances of growth. The

number of late injuries would be much greater if all patients irradiated for cancer lived.

Roentgenologists, technicians, physicists and workers in roentgen tube factories are subject to occupational injury by the rays. In diagnosis the physician may be injured by palpating behind the screen with his hands insufficiently protected. Dentists have been injured by holding films in the mouths of patients. Modern roentgen apparatus is quite safe but many small hospitals are still using apparatus that is dangerous to the physician and his assistants.

It is well known that individuals working much with roentgen rays show a certain degree of leucopenia and leucocytosis without any impairment of general condition. Regular blood examinations should be made to see that the change does not become excessive. It should be possible with care to prevent roentgen carcinoma, as it is always preceded by defects or ulcers. Surgeons whose hands are exposed to mechanical and chemical injuries are pre-disposed to late roentgen injury. Irradiation with red light (carbon arc light) gives good results in roentgen ulcers.

Injuries of the genital glands have been reported in physics teachers who have demonstrated before their classes with small apparatus. One student was injured who allowed his hand to be used for demonstration purposes because it contained a metallic foreign body. Roentgen injuries in tube factories have become very rare. The founder of the Müller tube factory died of roentgen injuries but for many years they have had no further injuries. The danger of occupational injury with modern apparatus and reasonable training and care on the part of the personnel has been reduced to a minimum.—*Audrey G. Morgan.*

Gambarow, G. Zur Frage der histologischen Veränderungen des Karziomgewebes nach Strahlenbehandlung. (Histological changes in carcinoma tissue after irradiation.) *Strahlentherapie*, 1931, *41*, 531–542.

In spite of careful histological examinations there are still many unsettled questions in regard to the finer changes that take place in tumor tissue after irradiation. The author gives detailed descriptions of the histological findings in 3 cases, 2 of superficial and 1 of deep carcinoma, illustrated by photomicrographs.

He finds that the primary changes are signs of degeneration and breaking down of tumor cells, while proliferation of connective tissue is secondary. It is questionable, however, whether these regressive changes, such as hydropic swelling, necrosis and cyst formation of the tumor cells, pycnosis of the nuclei, etc., develop after irradiation or whether they have already existed before treatment. In the author's third case there were various signs of degeneration before treatment. These signs increased after the irradiation. He has often seen changes in the mitotic figures in the form of clumping in non-irradiated sections, though some authors deny that such changes occur before irradiation. In addition to regressive changes there is a trace of cornification of the tumor cells in non-irradiated specimens.

There has been a discussion as to whether resting cells in the tumor undergo the same changes as karyokinetic ones, such as breaking up of the nuclei into fine granules and drops. Though he looked carefully the author could find no evidence that such changes take place in resting cells. He does not claim that resting cells are absolutely insensitive to the rays, but it is at least very difficult to demonstrate any changes in them.

It is generally believed that there is rapid destruction of leucocytes after irradiation, but the author doubts this. In one case he saw destruction of leucocytes soon after irradiation, but they increased later. Of course, definite conclusions cannot be drawn from this one case.

There does not seem to be any definite law in regard to the time of the reaction. After irradiation there was first decrease and then disappearance of mitoses, but no regularity in the time after which these changes occurred. He questions whether the three stages described by Alberti and Politzer are characteristic changes brought about by irradiation. There are differences in different tumors.

In one case the author irradiated one-half of a tumor with radium and the other half with roentgen rays. On the radium side round cell infiltration was decidedly more intense than on the roentgen side. Radium also increased the number of mitoses more than roentgen rays did. Otherwise there was no decided difference in the histological pictures, but a year after complete healing of the carcinoma there was a recurrence in the roentgen side and none on the radium side.

He found that full doses and divided doses give the same result. Hamperl and Schwarz came to the same conclusion from their examinations.—*Audrey G. Morgan.*